Devi, S.
10/009792

(FILE 'CAPLUS' ENTERED AT 14:04:57 ON 12 OCT 2004)
L1 1 S PTHKCSFM?

- key terms

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 07 Oct 2001
ACCESSION NUMBER: 2001:731048 CAPLUS
DOCUMENT NUMBER: 135:283966
TITLE: Plasmid vectors and recombinant production of human granulocyte colony stimulating factor (G-CSF) in Escherichia coli
INVENTOR(S): Lee, Sang-Yup; Jeong, Ki-Jun
PATENT ASSIGNEE(S): Korea Advanced Institute of Science and Technology, S. Korea
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001073081	A1	20011004	WO 2001-KR549		20010331
W: CN, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
EP 1185675	A1	20020313	EP 2001-922090		20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
US 2003153049	A1	20030814	US 2001-9792		20011213
PRIORITY APPLN. INFO.:			KR 2000-17052	A	20000331
			WO 2001-KR549	W	20010331

AB The invention relates to construction of plasmid vectors and methods to recombinant production of human granulocyte colony stimulating factor (G-CSF)
in E.coli. The present invention provides a recombinant plasmid vector comprising a kanamycin resistance gene, a promoter, an endoxylanase signal sequence, a nucleotide sequence coding for an oligopeptide consisting of 13 amino acids including 6 consecutive histidine residues, and a human granulocyte colony stimulating factor (hG-CSF) gene. The lower G-C content in N-terminal portion of hG-CSF is created due to inhibitory effect of high G+C content in N-terminal of hG-CSF on transcription and translation. The signal sequence od endoxylanase derived from Bacillus sp. is used for the secretion of hG-CSF protein from E.coli. The present invention also provides an E. coli transformed with the said vector and a process for producing complete hG-CSF protein with high purity from the protein pool secreted by the said microorganism. In accordance with the invention, the hG-CSF protein can be prepared with high purity through rather simple process facilitating secretion of large amount of hG-CSF fusion protein into the periplasm, which does not require complicated processes such as solubilization and subsequent refolding required for isolation of the hG-CSF protein produced in cytoplasm as insol. inclusion bodies by conventional techniques. The hG-CSF protein prepared by this methods can be widely used as an active ingredient in the development of supplementary agents for anticancer therapy.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 14:07:21 ON 12 OCT 2004)
L2 1 S L1

L2 ANSWER 1 OF 1 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-616523 [71] WPIDS
DOC. NO. CPI: C2001-184666
TITLE: Recombinant plasmid vector comprising an endoxylanase signal sequence, human granulocyte colony stimulating factor gene and other components, when transformed into microorganism useful for preparing the colony stimulating factor.
DERWENT CLASS: B04 D16
INVENTOR(S): JEONG, K; LEE, S; JUNG, G J; LEE, S Y; CHUNG, G J
PATENT ASSIGNEE(S): (KOAD) KOREA ADV INST SCI & TECHNOLOGY; (JEON-I) JEONG K; (LEES-I) LEE S
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001073081	A1	20011004	(200171)*	EN	50
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: CN US					
KR 2001094652	A	20011101	(200223)		
EP 1185675	A1	20020313	(200225)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					
CN 1366551	A	20020828	(200282)		
KR 358948	B	20021031	(200329)		
US 2003153049	A1	20030814	(200355)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001073081	A1	WO 2001-KR549	20010331
KR 2001094652	A	KR 2000-17052	20000331
EP 1185675	A1	EP 2001-922090	20010331
		WO 2001-KR549	20010331
CN 1366551	A	CN 2001-800753	20010331
KR 358948	B	KR 2000-17052	20000331
US 2003153049	A1	WO 2001-KR549	20010331
		US 2001-9792	20011213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1185675	A1 Based on	WO 2001073081
KR 358948	B Previous Publ.	KR 2001094652

PRIORITY APPLN. INFO: KR 2000-17052 20000331
AN 2001-616523 [71] WPIDS
AB WO 200173081 A UPAB: 20011203

Searcher : Shears 571-272-2528

NOVELTY - A recombinant plasmid vector (I) comprising a kanamycin resistance gene (II), a promoter (III), an endoxylanase signal sequence (IV), a nucleotide sequence (V) coding for an oligopeptide consisting of 13 amino acids including 6 consecutive histidine residues, and a human granulocyte colony stimulating factor (hG-CSF) gene (VI), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a microorganism, Escherichia coli transformed with (I), which is **pTHKCSFmII** comprising (II), a Trc promoter, an endoxylanase signal sequence derived from Bacillus sp., a nucleotide sequence coding for an oligopeptide having a sequence AGPHHHHHHIEGR and a modified gene coding for a human granulocyte colony stimulating factor (hG-CSF), which includes a nucleotide sequence of 180 bp as given in the specification, at the N-terminus.

USE - E.coli transformed with (I) is useful for preparing human granulocyte colony stimulating factor. The method comprises culturing the microorganism to obtain a human granulocyte colony stimulating factor fusion protein and treating the fusion protein with a protease preferably Factor Xa, to obtain a human granulocyte colony stimulating factor, where the fusion protein is obtained from the culture by employing Ni-column (claimed).

ADVANTAGE - E.coli transformed with (I) facilitates the secretion of large amount of hG-CSF fusion protein into the periplasm, which does not require complicated processes such as solubilization and subsequent refolding required for isolation of the hG-CSF protein produced in cytoplasm as insoluble inclusion bodies by conventional techniques, thus, the hG-CSF protein can be widely used as an active ingredient in the development of supplementary agents for anticancer therapy.

Dwg.0/13

(FILE 'CAPLUS' ENTERED AT 14:08:10 ON 12 OCT 2004)

L3	1111	SEA FILE=CAPLUS ABB=ON PLU=ON HGCSF OR (HG OR HUMAN GRANULOCYT?)(W)(CSF OR COLONY STIMUL?)
L6	666	SEA FILE=CAPLUS ABB=ON PLU=ON RHGCSF OR (RHUG OR RHG)(W)(CSF OR COLONY STIMUL?)
L7	1106	SEA FILE=CAPLUS ABB=ON PLU=ON HUMAN(W)(GCSF OR GRANULOCYT?(W)(CSF OR COLONY STIMUL?))
L8	821	SEA FILE=CAPLUS ABB=ON PLU=ON (L3 OR L7)(S)RECOMBINAN?
L9	38	SEA FILE=CAPLUS ABB=ON PLU=ON (L6 OR L8) AND VECTOR
L10	20	SEA FILE=CAPLUS ABB=ON PLU=ON L9 AND PLASMID
L11	19	L10 NOT L1

L11 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

ED	Entered STN: 19 Aug 2004
ACCESSION NUMBER:	2004:678394 CAPLUS
DOCUMENT NUMBER:	141:201290
TITLE:	Development of highly efficient expression **vector** pNOS GKT2B-R for producing recombinant proteins in animal cell
INVENTOR(S):	Okabe, Masato; Nakamura, Tetsuo
PATENT ASSIGNEE(S):	Immuno Japan Inc., Japan
SOURCE:	PCT Int. Appl., 96 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004070030	A1	20040819	WO 2004-JP1066	20040203

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2003-25677 A 20030203

AB Highly efficient expression **vector** pNOS GKT2B-R for producing recombinant proteins in animal cell has been developed. The use of the **vector** enables the expression in the animal cells of the protein that cannot be produced in bacterial, microbial eukaryotic or insect cells. The **plasmid** is consisted of potent expression-inducing promoter (human cytomegalo virus Major Immediately-Early antigen promoter, CMV5 synthetic chimera promoter, β-actin promoter or SV40 early promoter), multi-cloning sites, polyadenylation signal and promoter-less drug resistance gene. The promoter-less drug resistance genes used can be selected among neomycin-, codon disoptimized neomycin-, hygromycin-, zeocin- and blasticidin-resistance genes. The neomycin-resistance gene is the E. coli transposon Tn5-derived gene for neomycin phosphotransferase. Antibiotics resistance gene expression is designed to be min. by being placed polyadenylation signal downstream. Promoter-less or disoptimized dihydrofolate reductase gene is placed at antibiotics resistance gene downstream. The dihydrofolate reductase gene is designed to be driven by a weak promoter. Transformants that can produce recombinant proteins during serum-free culture can be obtained by transfection with the constructed **vector** containing transgene inserted at the cloning site. The **vector** is typically introduced to the CHO cells with dihydrofolate reductase deficiency and propagated by the culture in the presence of methotrexate. **Plasmid** pNOS GKT2B-R containing gene for human G-CSF was constructed and introduced into the CHO cells to produce high level G-CSF (≥0.25 μg/μl). The G-CSF transgene in the produced G418-resistant CHO cell pNOS GKT2B-R transformant was demonstrated to be amplified in the culture with methotrexate and the G-CSF production level was 117 μg/mL/3 days.

L11 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 24 Jan 2001
ACCESSION NUMBER: 2001:55933 CAPLUS
DOCUMENT NUMBER: 135:29608
TITLE: **Recombinant human granulocyte colony-stimulating** factor expressed in escherichia coli
AUTHOR(S): Wu, Yin; Yang, Hong; Lu, Jun; Hu, Bo; Ma, Tonghui; Li, Yuxin; Hao, Shui

CORPORATE SOURCE: Institute of Genetics and Cytology, Northeast Normal University, Changchun, 130024, Peop. Rep. China
SOURCE: Dongbei Shida Xuebao, Ziran Kexueban (2000), 32(4), 46-51
CODEN: DSZKEE; ISSN: 1000-1832
PUBLISHER: Dongbei Shifan Daxue Xueshu Qikanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The primers were designed based on gene sequence of natural granulocyte colony-stimulating factor (G-CSF). G-CSF cDNA was prepared from the mRNA of mononuclear cells from human peripheral blood by RT-PCR. The cDNA was inserted into a prokaryotic expression **vector** pT7 to obtain the recombinant **plasmid**. The expression level of the E. coli containing natural human G-CSF cDNA was not satisfied. The reason that the high expression level was not easily reached in E. coli may be that the G/C ratio at 5' end of human G-CSF cDNA was too high, the transcribed mRNA was liable to form secondary structure, and then affected the beginning of transcription. The codons of G-SCF cDNA were changed by redesigning PCR primers on the principle of codon degeneracy, and a new **rhG-CSF** cDNA mutant was obtained. The expression of **rhG-CSF** was increased in E. coli transformed with the recombinant **plasmid** of the mutant.

L11 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 19 Jan 2001
ACCESSION NUMBER: 2001:50831 CAPLUS
DOCUMENT NUMBER: 134:114851
TITLE: Modified **human granulocyte-colony stimulating** factor and its production by **recombinant** expression in transformed Escherichia coli
INVENTOR(S): Kwon, Se Chang; Jung, Sung Youb; Bae, Sung Min; Lee, Gwan Sun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004329	A1	20010118	WO 2000-KR733	20000707
W: AU, BR, CA, CN, JP, NZ, RU, SG, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
KR 2001009171	A	20010205	KR 1999-27418	19990708
BR 2000012265	A	20020312	BR 2000-12265	20000707
EP 1194575	A1	20020410	EP 2000-942494	20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2003504069	T2	20030204	JP 2001-509533	20000707
AU 757147	B2	20030206	AU 2000-57106	20000707
AU 2000057106	A5	20010130		
NZ 516476	A	20030926	NZ 2000-516476	200007

RU 2232772	C2	20040720	RU 2002-103159	20000707
PRIORITY APPLN. INFO.:			KR 1999-27418 A	19990708
			WO 2000-KR733 W	20000707

AB Modified human granulocyte-colony stimulating factors (hG-CSF) are produced by culturing Escherichia coli transformed with expression **vectors** comprising a gene encoding a modified hG-CSF to produce and secrete the modified hG-CSF to periplasm. The modified hG-CSFs being obtained replacing at least one of the 1st, 2nd, 3rd and 17th amino acids of wild-type hG-CSF with another amino acid. Expression of hG-CSF variants is enhanced by construction of chimeric genes comprising sequences encoding the Escherichia coli wild-type or modified thermoresistant enterotoxin II signal peptide, the E. coli β-lactamase signal peptide, or the E. coli gene III signal peptide, as well as use of the Shine-Dalgano sequence from E. coli enterotoxin II gene.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 17 Aug 2000
ACCESSION NUMBER: 2000:569490 CAPLUS
DOCUMENT NUMBER: 134:290861
TITLE: **Plasmid** stability in long-term hG-CSF production using L-arabinose promoter system of Escherichia coli
AUTHOR(S): Choi, Seung-Jin; Park, Doo-Hong; Chung, Soo-Il; Jung, Kyung-Hwan
CORPORATE SOURCE: Mogam Biotechnology Research Institute, Kyonggi-Do, 449-910, S. Korea
SOURCE: Journal of Microbiology and Biotechnology (2000), 10(3), 321-326
CODEN: JOMBES; ISSN: 1017-7825
PUBLISHER: Korean Society for Applied Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To examine the feasibility of the long-term production of the human granulocyte colony stimulating factor (hG-CSF) using the L-arabinose promoter system of Escherichia coli, flask relay culture and cyclic fed-batch culture were performed. In the flask relay culture, it was found that the **plasmid** was maintained stably up to about 170 generations in an uninduced condition, whereby the cells could also maintain the capability of expressing hG-CSF upon induction. However, in an induced condition, the structural damage of the **plasmid** occurred after about 100 generations, and thereafter the hG-CSF expression decreased gradually. In both cases, it was observed that the **plasmid** and the hG-CSF expression were maintained stably up to at least 100 generations. In contrast, in the cyclic fed-batch culture, segregational **plasmid** instability was observed within about 4 generations after induction, even though the cell growth and hG-CSF production reached their maximum values, 78.0 g/l of dry cell weight and 7.0 g/l of hG-CSF, resp. It would appear that, when compared to the flask relay culture, the high-cell d. and high-level expression of hG-CSF in the cyclic fed-batch culture led to the segregational **plasmid** instability; in other words, a severe metabolic burden existed on the cells due to the high-level expression of hG-CSF. Accordingly, based on these long-term cultures, the segregational and structural **plasmid** instability was observed and a

strategy to overcome such problems could be designed.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 May 2000
ACCESSION NUMBER: 2000:350389 CAPLUS
DOCUMENT NUMBER: 132:318603
TITLE: **Recombinant plasmid** DNA pGGF-8 encoding a polypeptide showing properties of **human granulocytic colony-stimulating** factor and Escherichia coli - strain producer of the polypeptide showing properties of **human granulocytic colony-stimulating** factor
INVENTOR(S): Korobko, V. G.; Shingarova, L. N.; Petrovskaya, L. E.; Petrenko, L. A.; Pustoshilova, N. M.
PATENT ASSIGNEE(S): Gosudarstvennyi Nauchnyi Tsentr Virusologii i Bioteknologii "Vektor", Russia; Institut Bioorganicheskoi Khimii im.M.M.Shemyakina i Yu.A.Ovchinnikova
SOURCE: Russ. From: Izobreteniya 1998, (17), 267. CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2113483	C1	19980620	RU 1996-113021	19960621
PRIORITY APPLN. INFO.:			RU 1996-113021	19960621

AB Title only translated.

L11 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 Feb 2000
ACCESSION NUMBER: 2000:106551 CAPLUS
DOCUMENT NUMBER: 132:246682
TITLE: Biological activity of human granulocyte colony stimulating factor with a modified C-terminus
AUTHOR(S): Oshima, Yasuo; Tojo, Arinobu; Niho, Yoshiyuki; Asano, Shigetaka
CORPORATE SOURCE: Department of Hematology and Oncology, Institute of Medical Science, University of Tokyo, Tokyo, 108-8639, Japan
SOURCE: Biochemical and Biophysical Research Communications (2000), 267(3), 924-927 CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Granulocyte colony-stimulating factor (G-CSF) undergoes receptor-mediated internalization into target cells which are normally restricted to neutrophilic granulocytes and their committed progenitor cells, suggesting that it may be applicable as a myeloid cell-targeting vehicle. To test this notion, the authors constructed a cDNA encoding a human G-CSF/murin

stem cell factor (mSCF) chimeric mol. in a mammalian expression **vector** and transfected NIH3T3 cells with this **plasmid.** The resulting chimeric cytokine consisted of the entire G-CSF sequences fused to Lys 148 of mSCF. It can be released from the surface membrane of NIH3T3 transformants through proteolytic cleavage at Ala 164 of mSCF. The culture media conditioned by a number of stable transformants, which were confirmed by an ELISA to secrete an hG-CSF derivative, were examined for their ability to stimulate CFU-G-derived colony formation as well as the proliferation of G-CSF-dependent NFS-60 cells. The results indicated that this C-terminus modified version of **hG-CSF** is as potent as **recombinant hG-CSF** in both assays.
(c) 2000 Academic Press.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 Aug 1999
ACCESSION NUMBER: 1999:499914 CAPLUS
DOCUMENT NUMBER: 131:267696
TITLE: Novel Secretion System of Recombinant Saccharomyces cerevisiae Using an N-terminus Residue of Human IL-1β as Secretion Enhancer
AUTHOR(S): Lee, Jeewon; Choi, Seong-Il; Jang, Jun Sung; Jang, Kiryong; Moon, Jae Woong; Bae, Cheon Soon; Yang, Doo Suk; Seong, Baik Lin
CORPORATE SOURCE: Biochemical Process Engineering R.U., Korea Research Institute of Bioscience and Biotechnology (KRIBB), Yusong Taejon, 305-600, S. Korea
SOURCE: Biotechnology Progress (1999), 15(5), 884-890
CODEN: BIPRET; ISSN: 8756-7938
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An N-terminal sequence of human interleukin 1β (hIL-1β) was used as a fusion expression partner for the production of two **recombinant** therapeutic proteins, **human granulocyte-colony stimulating** factor (**hG-CSF**) and human growth hormone (hGH), using Saccharomyces cerevisiae as a host. The expression cassette comprised the leader sequence of killer toxin of Kluyveromyces lactis, the N-terminal 24 amino acids (Ser5-Ala28) of mature hIL-1β, the KEX2 dibasic endopeptidase cleavage site, and the target protein (hG-CSF or hGH). The gene expression was controlled by the inducible UASgal/MF-α1 promoter. With the expression **vector** above, both recombinant proteins were well secreted into culture medium with high secretion efficiencies, and especially, the recombinant hGH was accumulated up to around 1.3 g/L in the culture broth. This is due presumably to the significant role of fused hIL-1β as secretion enhancer in the yeast secretory pathway. In our recent report, various immunoblotting analyses have shown that the presence of a core N-glycosylation resident in the hIL-1β fragment is likely to be of crucial importance in the high-level secretion of **hG-CSF** from the **recombinant** S. cerevisiae. When the N-glycosylation was completely blocked with the addition of tunicamycin to the culture, the secretion of hG-CSF and hGH was decreased to a negligible level although

the other host-derived proteins were well secreted to the culture broth regardless of the presence of tunicamycin. The N-terminal sequencing of the purified hG-CSF verified that the hIL-1β fusion peptide was correctly removed by in vivo KEX2 protease upon the exit of fusion protein from Golgi complex. From the results presented in this article, it is strongly suggested that the N-terminal fusion of the hIL-1β peptide could be utilized as a potent secretion enhancer in the expression systems designed for the secretory production of other heterologous proteins from S. cerevisiae.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 17 Dec 1998
ACCESSION NUMBER: 1998:790676 CAPLUS
DOCUMENT NUMBER: 130:24141
TITLE: Manufacture of **human granulocyte colony-stimulating** factor with **recombinant** Escherichia coli
INVENTOR(S): Jun, Hyung-kyun; Choi, Bong-woong; Lee, Young-ik; Sohn, Mi-jin
PATENT ASSIGNEE(S): Korea Research Institute of Bioscience and Biotechnology, S. Korea; Jeil Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853072	A1	19981126	WO 1998-KR125	19980521
W: CN, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			KR 1997-20054	19970522

AB The present invention relates to the production of human granulocyte colony-stimulating factor (hG-CSF). A **recombinant plasmid** pYHM-G-CSF containing cDNA for PelB signal peptide-**hG-CSF** was produced and introduced into Escherichia coli. The **recombinant** bacteria produced 1.7g PelB-**hG-CSF** from 1L culture media. The refolded and purified PelB-hG-CSF has the biol. activity of G-CSF.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 03 Dec 1998
ACCESSION NUMBER: 1998:756773 CAPLUS
DOCUMENT NUMBER: 130:76809
TITLE: Over-expression of G-CSF in Escherichia coli and fast purification protocol
AUTHOR(S): Li, Fu-Sheng; Gong, Hui-Yu; Zhao, Bing-Wen; Yu, Cai-Ling; Hou, Bin; Chen, Ai-Jun; Zhang, Zhi-Qing; Hou, Yun-De

CORPORATE SOURCE: State Key Lab. Mol. Virol. Genetic Eng., Inst. Virol. CAPM, Beijing, 100052, Peop. Rep. China
SOURCE: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao (1998), 14(5), 479-484
CODEN: ZSHXF2; ISSN: 1007-7626
PUBLISHER: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao Bianweihui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB **Recombinant human granulocyte colony stimulating** factor (**rhG-CSF**) is mainly used in neutropenia induced by cytotoxic chemotherapy in clin. practice. After a Chinese human G-CSF cDNA was cloned, the 5' terminal sequence in G-CSF cDNA was thoroughly modified in order to raise the expression level. **Plasmid** pBV220/G-CSF/2-174 was constructed by inserting the modified gene into the pBV220 **vector**. Over 50% of the cellular protein was the **rhG-CSF**. As G-CSF was in inclusion body in E. coli, a simple and stable purification protocol was established, which was very suitable for large-scale purification Firstly, inclusion body was extracted from E. coli, and then, 8 mol/L urea was used to lysis the inclusion body. G-CSF protein was renatured by dilution And the pure G-CSF was recovered by one-step SP-Sepharose FF chromatog. The relative activity of purified G-CSF reached to 3.4 x 108 U/mg protein. A total G-CSF activity from 1 L fermentation was about 1.06 x 1011 U. As demonstrated by N-terminal amino acid sequencing, methionine had thoroughly been removed, so this kind of purified G-CSF may have a low immunogenicity and toxicity.

L11 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 04 May 1998
ACCESSION NUMBER: 1998:252165 CAPLUS
DOCUMENT NUMBER: 128:317751
TITLE: **Recombinant** expression and identification of **human granulocyte colony-stimulating** factor cDNA in Escherichia coli
AUTHOR(S): Fang, Xiangdong; Ma, Li; Gao, Jimin; Huang, Shuqi; Wang, Xiaoning
CORPORATE SOURCE: Institute Molecular Immunology, First Military Medical Univ., Canton, 510515, Peop. Rep. China
SOURCE: Zhongguo Shenghua Yaowu Zazhi (1998), 19(1), 1-5
CODEN: ZSYZFP; ISSN: 1005-1678
PUBLISHER: Zhongguo Shenghua Yaowu Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The gene for human granulocyte colony-stimulating factor (G-CSF) was amplified by RT-PCR and inserted into the expression **vector** pJGW1. The **recombinant** human G-CSF (**rhG-CSF**) was expressed in E. coli DH5α that contained **plasmid** pJGW1-**hG-CSF** and pGP1-2. G-CSF (mol. weight .apprx.19 kilodaltons) accounted for >30% of total protein of the recombinant E. coli. Western-blot revealed that the 19-kilodalton protein shared specific antigenicity with native G-CSF. The **rhG-CSF** was isolated and purified up to 98% purity by inclusion body isolation, refolding and CM-Sepharose Fast Flow ion exchange chromatog.

L11 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 11 Apr 1997
ACCESSION NUMBER: 1997:234862 CAPLUS
DOCUMENT NUMBER: 126:272945
TITLE: Expression of human granulocyte colony stimulating factor gene in insect cells
AUTHOR(S): Chen, Hongxing; Qin, Junchuan; Zhu, Jie; Zhang, Yuhai; Jian, Ruiqing
CORPORATE SOURCE: Department of Biochemistry, Nanjing University, Nanjing, Peop. Rep. China
SOURCE: Nanjing Daxue Xuebao, Ziran Kexue (1996), 32(4), 616-620
CODEN: NCHPAZ; ISSN: 0469-5097
PUBLISHER: Nanjing Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A **plasmid** pBlueBac-G-CSF containing **human granulocyte colony stimulating** factor (**hG-CSF**) gene was constructed and co-transfected into Spodoperta frugiperda cells by **vector** Autographa californica nuclear polyhidrosis virus (AcNPV), and the **recombinant** virus was identified and purified by 4 rounds of blue-plague picking up. The culture medium was assayed, showing that the **recombinant** virus infected Sf9 and H5 cells expressing **hG-CSF** up to 1.5x106 and 1.9x106 CFU/mL, resp. The **recombinant hG-CSF** with apparent mol. mass of 19 KDa was detected by the western blot method. The results indicate that hG-CSF can be expressed in insect cells at high level and the expressed hG-CSF has the same character as the natural one.

L11 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 24 Mar 1997
ACCESSION NUMBER: 1997:194362 CAPLUS
DOCUMENT NUMBER: 126:195876
TITLE: Overexpression study of human colony stimulating factors in Escherichia coli. 2. Overexpression of human granulocyte colony stimulating factor
AUTHOR(S): Chmeliauskaite, V.; Miksyt, R.; Luksa, V.; Zvirblis, G.; Zareckaja, E.
CORPORATE SOURCE: Institute of Biotechnology, Vilnius, 2028, Lithuania
SOURCE: Biologija (1996), (2), 15-18
CODEN: BOLOE8; ISSN: 1392-0146
PUBLISHER: Academia
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An E. coli strain capable of producing the **recombinant human granulocyte colony stimulating** factor (**hG-CSF**) protein with an expression rate in the range of 30-40% of total cellular protein was developed. The target protein synthesis is under the two-step control of T7 and lac promoters. Methionine was added to the N-terminal sequence of the hG-CSF. Recombinant protein is accumulated in an insol. form (inclusion bodies) within the cell cytoplasm.

L11 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 08 May 1996
ACCESSION NUMBER: 1996:269618 CAPLUS
DOCUMENT NUMBER: 124:333929
TITLE: Construction of **hG-CSF** cDNA **recombinant** retrovirus
AUTHOR(S): Qu, Chengkui; Wei, Handong; He, Fuchu; Xu, Li; Wu, Zuze
CORPORATE SOURCE: Inst. of Radiation medicine, Acad. of Military Medical Sci., Beijing, 100850, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (1995), 19(4), 241-4
CODEN: JYKYEL; ISSN: 1000-5501
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Human granulocyte colony-simulating factor (**hG-CSF**) cDNA with non-coding region was recombined with retrovirus **vector** pLXSN through DNA **recombinant** techniques. After this, the **plasmid** was transfected into the retrovirus packing cell line PA317. **HG-CSF** cDNA was integrated and expressed in **recombinant** retrovirus-infected cells.

L11 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Jul 1995
ACCESSION NUMBER: 1995:693426 CAPLUS
DOCUMENT NUMBER: 123:76436
TITLE: Expression system for **recombinant** **human granulocyte-colony** **stimulating** factor in eukaryotic cell lines
INVENTOR(S): Mele, Antonio; Rotondaro, Luigi
PATENT ASSIGNEE(S): Menarini Ricerche Sud S.p.A., Italy
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511982	A1	19950504	WO 1994-EP3488	19941024
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9479395	A1	19950522	AU 1994-79395	19941024
PRIORITY APPLN. INFO.:			IT 1993-FI212	19931025
			WO 1994-EP3488	19941024

AB A process is disclosed for the preparation of **recombinant** **human granulocyte-colony stimulating** factor (G-CSF) for which is used a **vector** system which comprises at least one of the following elements: (1) a cytomegalovirus (CMV) promoter upstream of a DNA sequence encoding the desired protein, (2) a sequence for processing of RNA transcripts, and (3) a selection and amplification marker sequence. Thus a human G-CSF expression

vector was prepared in which the 3'-untranslated region of the mRNA containing AUUUA repeated motifs is removed in order to give a high level of protein production The sequence encoding hG-CSF was then cloned into **plasmids** containing, the murine or human cytomegalovirus major immediate-early promoter, and the rabbit β1-globin gene second intron and polyadenylation site. The SV1DHFR transcription unit from com. available **plasmid** pSV2dhfr was inserted to provide a selection marker. High levels of protein were expressed in transfected CHO dhfr- cells. Such recombinant human G-CSF can be used for the preparation of pharmaceutical compns. for promoting hematopoiesis, for the augmentation of the defense mechanism against infection, and for the stimulation and hyperprodn. of functionally primed effector cells against malignant diseases.

L11 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Nov 1994
ACCESSION NUMBER: 1995:9309 CAPLUS
DOCUMENT NUMBER: 122:24808
TITLE: Cloning of human granulocyte colony-stimulating factor cDNA and its expression in Escherichia coli
AUTHOR(S): Zhu, Shenggeng; Qin, Shulin; Wang, Aixia; Xiao, Zhizhuang; Guo, Zhenquan; Huang, Yixiu; Zhang, Lei
CORPORATE SOURCE: Dep. Biol., Peking Univ., Beijing, Peop. Rep. China
SOURCE: Beijing Daxue Xuebao, Ziran Kexueban (1993), 29(6), 675-9
CODEN: PCTHAP; ISSN: 0479-8023
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Monocytes were isolated from freshly prepared peripheral blood of a healthy adult human and were stimulated by lipopolysaccharide (LPS) to produce hG-CSF. The hG-CSF appeared in culture after 12 h induction and was maximal through 24 h. Total RNA was isolated from human monocytes induced by LPS by using acid guanidinium-phenol-chloroform extraction and amplified specifically by reverse transcription-PCR to obtain hG-CSF cDNA. The optimal annealing temperature determined exptl. was 57°, at which the reaction product for hG-CSF cDNA was maximized and non-specific products were reduced. The hG-CSF cDNA was inserted into the secretion expression **vector** pIN-ompA reformed by the laboratory, and then transformed into competent E. coli. Recombinant **plasmids** were identified by restriction enzyme assay and Southern hybridization with 3'-terminal, 5'-terminal, and middle sequence probes. After induction using IPTG, the **hG-CSF** protein was detected in the periplasmic space of the **recombinant** E. coli cells. Thus, hG-CSF cDNA was cloned and expressed in E. coli.

L11 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 21 Aug 1993
ACCESSION NUMBER: 1993:464004 CAPLUS
DOCUMENT NUMBER: 119:64004
TITLE: Polypeptide derivatives of human granulocyte colony-stimulating factor and monoclonal antibody
INVENTOR(S): Yoshida, Hajime
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: U.S., 55 pp. Cont.-in-part of U.S. Ser. No. 136,647, abandoned.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5194592	A	19930316	US 1989-318527	19890303
JP 10052281	A2	19980224	JP 1997-114630	19871223
JP 01225495	A2	19890908	JP 1988-51357	19880304
US 5214132	A	19930525	US 1989-337002	19890412
US 5362853	A	19941108	US 1992-994924	19921222
US 6027720	A	20000222	US 1994-274433	19940713
US 5681720	A	19971028	US 1995-434411	19950503
US 5714581	A	19980203	US 1995-434402	19950503
US 5795968	A	19980818	US 1997-783288	19970110
US 5994518	A	19991130	US 1997-890640	19970709

PRIORITY APPLN. INFO.:

JP 1986-306799	A	19861223
US 1987-136647	B2	19871222
JP 1988-51357	A	19880304
JP 1988-80088	A	19880331
JP 1994-185787	A3	19871223
US 1989-318527	A2	19890303
US 1989-337002	A3	19890412
US 1992-994924	A3	19921222
US 1994-274433	A3	19940713
US 1995-434411	A3	19950503

AB **Recombinant human granulocyte colony -stimulating** factor (B-CSF) polypeptide derivs. are produced in Escherichia coli using modified cDNA fragments. The G-CSF derivs. preferably have ≥1 amino acid substitution among residues 1-17 from the N-terminus and/or ≥1 deletion among residues 1-11 from the N-terminus. Deletions may also be produced by enzymic degradation; susceptibility to serine protease may be increased by substitution of serine e.g. in position 17. The G-CSF derivs. have high specific G-CSF activity and high stability in blood, and are useful in promoting proliferation of hematopoietic stem cells and differentiation of neutrophils during anticancer therapy. Thus, G-CSF derivative ND28 ([Ala1, Thr2, Tyr4, Arg5, Ser17]G-CSF) was produced by E. coli transformed with a **plasmid** containing G-CSF cDNA prepared from normal human peripheral blood macrophages, altered by insertion of a DNA linker mixture, and selected for ampicillin resistance. ND28 was purified by affinity chromatog. on an immobilized IgG1 monoclonal antibody (KM-498) to ND28.

L11 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 Dec 1992
ACCESSION NUMBER: 1992:639827 CAPLUS
DOCUMENT NUMBER: 117:239827
TITLE: Polypeptide-polymer conjugate continuous-release pharmaceutical compositions
INVENTOR(S): Camble, Roger; Timms, David; Wilkinson, Anthony James
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Brit. UK Pat. Appl., 206 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2246295	A1	19920129	GB 1991-15207	19910715
GB 2246295	B2	19940511		
FI 9103410	A	19920124	FI 1991-3410	19910715
EP 473268	A2	19920304	EP 1991-306452	19910716
EP 473268	A3	19920916		
EP 473268	B1	20031008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9105555	A	19920429	ZA 1991-5555	19910716
AT 251641	E	20031015	AT 1991-306452	19910716
CA 2047540	AA	19920124	CA 1991-2047540	19910722
AU 9181238	A1	19920130	AU 1991-81238	19910722
AU 655187	B2	19941208		
HU 60632	A2	19921028	HU 1991-2442	19910722
JP 05032559	A2	19930209	JP 1991-271743	19910722
JP 3188292	B2	20010716		
US 5320840	A	19940614	US 1991-734225	19910722
US 5773581	A	19980630	US 1995-488457	19950607

PRIORITY APPLN. INFO.:

GB 1990-16138	A	19900723
GB 1990-18414	A	19900823
GB 1990-18415	A	19900823
GB 1990-18416	A	19900823
GB 1990-18417	A	19900823
GB 1990-18418	A	19900823
US 1991-734225	A3	19910722
US 1993-155327	B1	19931122

AB Pharmaceutical compns. for continuous release of an acid stable physiol. active substance (polypeptide) from material of the composition (e.g. polylactide or biodegradable hydrogel) into an aqueous physiol.-type environment, comprise a polypeptide covalently conjugated to a water soluble polymer and incorporated into a matrix of polylactide, etc.; the polypeptide is released over a period of ≥1 wk. **Human granulocyte colony-stimulating** factor (**hG-CSF**) and solution-stable derivs. thereof were prepared by **recombinant** DNA methods and conjugated with Me PEGs. Continuous-release pharmaceutical compns. contained the conjugates incorporated in polylactide (50 weight% D,L-lactide/50 weight% glycolide copolymer) matrix.

L11 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 24 Jun 1988
ACCESSION NUMBER: 1988:217269 CAPLUS
DOCUMENT NUMBER: 108:217269
TITLE: High-yield expression of modified human granulocyte colony-stimulating factor gene in yeast and Escherichia coli
INVENTOR(S): Cerretti, Douglas Pat; Cosman, David John; Gillis, Stephen; Mochizuki, Diane Yukiko; March, Carl Jack; Price, Virginia Lee; Tushinski, Robert J.; Urdal, David Lloyd
ENT ASSIGNEE(S): Immunex Corp., USA

SOURCE: Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 243153	A2	19871028	EP 1987-303509	19870422
EP 243153	A3	19880113		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8702705	A	19871230	ZA 1987-2705	19870415
DK 8702031	A	19871023	DK 1987-2031	19870421
JP 63000299	A2	19880105	JP 1987-98465	19870421
AU 8771844	A1	19871029	AU 1987-71844	19870422
AU 601727	B2	19900920		
PRIORITY APPLN. INFO.:			US 1986-856643	19860422
			US 1986-931458	19861114

AB **Human granulocyte colony-stimulating factor (hG-CSF)** derivs. are **recombinantly** produced in high yields in yeast and Escherichia coli hosts. **Plasmid** pBC102.K22 was constructed containing a site-specifically mutagenized hG-CSF gene (having the codon for arginine at position 22 replaced with that for lysine such that a KEX2 protease-sensitive site is eliminated) linked at the 5'-end via a KEX2 recognition site to an α-factor leader sequence and a sequence encoding an antigenic peptide capable of cleavage by bovine enterokinase. Yeast transformed with pBC102.K22 showed 5-fold higher expression than yeast transformed with **vector** containing native hG-CSF protein gene.

L11 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 27 Nov 1987
ACCESSION NUMBER: 1987:596517 CAPLUS
DOCUMENT NUMBER: 107:196517
TITLE: Preparation and use of a human granulocyte colony-stimulating factor for the treatment of leukopenia
INVENTOR(S): Tamura, Masahiko; Nomura, Hitoshi; Hattori, Kunihiro; Ono, Masayoshi
PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 217404	A2	19870408	EP 1986-113671	19861003
EP 217404	A3	19880713		
EP 217404	B1	19920115		
EP 217404	B2	19990107		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
JP 62174026	A2	19870730	JP 1986-125660	19860602

JP 06018778	B4	19940316		
AU 8663121	A1	19870409	AU 1986-63121	19860924
AU 596997	B2	19900524		
ZA 8607410	A	19870527	ZA 1986-7410	19860929
FI 8603971	A	19870405	FI 1986-3971	19861001
DK 8604713	A	19870405	DK 1986-4713	19861002
DK 172204	B1	19980105		
NO 8603918	A	19870406	NO 1986-3918	19861002
AT 71662	E	19920215	AT 1986-113671	19861003
ES 2055684	T3	19940901	ES 1986-113671	19861003
PRIORITY APPLN. INFO.:			JP 1985-220450	19851004
			JP 1986-125660	19860602
			EP 1986-113671	19861003

AB **Human granulocyte colony-stimulating** factors (G-CSF) are obtained by isolation from the supernatant of a culture of a human G-CSF-producing cell or by transformation of a host with a **recombinant vector** having a gene coding for a polypeptide with human G-CSF activity. These factors are leukopenia treating agents. Specific sequences are also given for the gene coding for the G-CSF-active polypeptide. An oral cavity cancer tumor of a patient with a pronounced increase in the number of neutrophils was transplanted into nu/nu mice. Twelve days later, the tumor was extracted aseptically, dissected into cubes of 1-2 mm3 and cultured as follows. Ten-15 cubes were treated with trypsin for 10 min at 37° and again for 15 min before bovine fetal serum inactivation of enzyme. The process was repeated and the cells were incubated in a CO2 incubator (5% CO2 and 100% humidity) with an F-10 culture solution containing 10% bovine fetal serum.

The cells were further treated with mouse erythrocyte antibody and guinea pig complement, cultivated with the F-10 culture solution for 2 more days, and then subjected to cloning by the limiting dilution method. Clone CHU-2 exhibited CSF activity .apprx.10 x as high as that of the other clones. Human G-CSF was isolated from the supernatant by ultrafiltration, gel filtration on Ultrogel AcA54, HPLC on μ-Bondapak C18 of a 30% n-propanol-0.1% trifluoroacetic acid-soluble fraction, and HPLC on TSK-G 3000SW. Mice were s.c. injected daily with 0.1 mL of a physiol. saline solution containing n-propanol 1%, C57BL/6N mouse serum 10%, and human G-CSF 2.5 μg until blood sampling was conducted. After 14 days the CSF-treated group had 5359±584 compared with 1311±197 neutrophils/mm3 for controls ($p<0.001$).

L12	348	SEA	FILE=CAPLUS	ABB=ON PLU=ON	HUMAN(W)(G(W)(CSF OR COLONY STIMUL?))
L13	172	SEA	FILE=CAPLUS	ABB=ON PLU=ON	L12(S)RECOMBINAN?
L14	6	SEA	FILE=CAPLUS	ABB=ON PLU=ON	L13 AND VECTOR
L15	5	SEA	FILE=CAPLUS	ABB=ON PLU=ON	L14 AND PLASMID
L16	2	L15 NOT (L1 OR L11)			

L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 29 Jun 2003
ACCESSION NUMBER: 2003:492424 CAPLUS
DOCUMENT NUMBER: 139:74025
TITLE: G-CSF conjugates for therapeutic uses

Searcher : Shears 571-272-2528

INVENTOR(S): Nissen, Torben Lauesgaard; Andersen, Kim Vilbour; Hansen, Christian Karsten; Mikkelsen, Jan Moller; Schambye, Hans Thalsgaard
PATENT ASSIGNEE(S): Maxygen Holdings Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp., Cont.-in-part of U.S. Ser. No. 904,196.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003118612	A1	20030626	US 2002-192294	20020710
US 2002004483	A1	20020110	US 2001-760008	20010110
US 6646110	B2	20031111		
US 2003064922	A1	20030403	US 2001-904196	20010711
US 6555660	B2	20030429		
ZA 2002004623	A	20021211	ZA 2002-4623	20020610

PRIORITY APPLN. INFO.:

DK 2000-24	A	20000110
US 2000-176376P	P	20000114
DK 2000-341	A	20000302
US 2000-189506P	P	20000315
DK 2000-943	A	20000616
US 2000-215644P	P	20000630
US 2001-760008	A2	20010110
US 2001-904196	A2	20010711
DK 2002-447	A	20020322
DK 2002-708	A	20020508

AB Polypeptide conjugates with G-CSF activity comprising a polypeptide having at least one introduced lysine residue and at least one removed lysine residue compared to the sequence of human G-CSF, and which are conjugated to 2-6 polyethylene glycol moieties are described. The conjugates have a low in vitro bioactivity, a long in vivo half-life, a reduced receptor-mediated clearance, and provide a more rapid stimulation of production of white blood cells and neutrophils than non-conjugated **recombinant human G-CSF**.

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 18 Dec 1996
ACCESSION NUMBER: 1996:742791 CAPLUS
DOCUMENT NUMBER: 126:70737
TITLE: Systemic hematological effects of granulocyte colony-stimulating factor produced by irradiated gene-transfected fibroblasts
AUTHOR(S): Rosenthal, Felicia M.; Kulmburg, Peter; Frueh, Reinhard; Pfeifer, Carolin; Veelken, Hendrik; Mackensen, Andreas; Koehler, Gabriele; Lindemann, Albrecht; Mertelsmann, Roland
CORPORATE SOURCE: Department Medicine I (Hematology/Oncology), University Medical Center Freiburg, Freiburg, 79106, Germany
SOURCE: Human Gene Therapy (1996), 7(17), 2147-2156
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Liebert

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although long-term expression of therapeutic mols. is necessary for the treatment of permanent deficiencies, short-term expression of therapeutic mols. inducing local or systemic effects is preferable in clin. situations where temporary substitution is the goal. One such clin. setting is the administration of hematopoietic growth factors in cancer chemotherapy-induced myelosuppression. Several **plasmid vectors** containing the human granulocyte colony-stimulating factor (G-CSF) gene under transcriptional control of different regulatory elements were constructed. In vitro production of G-CSF by nonvirally transfected murine fibroblast clones initially increased after lethal irradiation and was detectable for at least 12 days. We also demonstrate that a single injection of irradiated G-CSF-secreting fibroblasts leads to accelerated hematopoietic recovery and mobilization of committed peripheral blood progenitor cells equivalent to that achieved by twice daily s.c. administration of high doses of **recombinant human G-CSF**. Using dicistronic **vectors**, high levels of G-CSF secretion were also obtained in human fibroblasts.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 14:15:54 ON 12 OCT 2004)
L17 14 S L10
L18 8 S L15
L19 15 S (L17 OR L18) NOT L2
L20 10 DUP REM L19 (5 DUPLICATES REMOVED)

L20 ANSWER 1 OF 10 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:183768 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA13520283966M
TITLE: **Plasmid vectors** and **recombinant** production of **human granulocyte colony stimulating** factor (G-CSF) in Escherichia coli
AUTHOR(S): Lee, Sang-Yup; Jeong, Ki-Jun
CORPORATE SOURCE: ASSIGNEE: Korea Advanced Institute of Science and Technology
PATENT INFORMATION: WO 2001073081 A1 4 Oct 2001
SOURCE: (2001) PCT Int. Appl., 50 pp.
CODEN: PIXXD2.
COUNTRY: KOREA, REPUBLIC OF
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2001:731048
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020319
AB The invention relates to construction of **plasmid vectors** and methods to **recombinant** production of **human granulocyte colony stimulating** factor (G-CSF) in E.coli. The present invention provides a **recombinant plasmid vector** comprising a kanamycin resistance gene, a promoter, an endoxylanase signal sequence, a nucleotide sequence coding for an oligopeptide consisting of 13 amino acids including 6 consecutive

histidine residues, and a **human granulocyte colony stimulating** factor (**hG-CSF**) gene. The lower G-C content in N-terminal portion of hG-CSF is created due to inhibitory effect of high G+C content in N-terminal of hG-CSF on transcription and translation. The signal sequence od endoxylanase derived from Bacillus sp. is used for the secretion of hG-CSF protein from E.coli. The present invention also provides an E. coli transformed with the said **vector** and a process for producing complete hG-CSF protein with high purity from the protein pool secreted by the said microorganism. In accordance with the invention, the hG-CSF protein can be prepared with high purity through rather simple process facilitating secretion of large amount of hG-CSF fusion protein into the periplasm, which does not require complicated processes such as solubilization and subsequent refolding required for isolation of the hG-CSF protein produced in cytoplasm as insol. inclusion bodies by conventional techniques. The hG-CSF protein prepared by this methods can be widely used as an active ingredient in the development of supplementary agents for anticancer therapy.

L20 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	2000139751 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 10673392
TITLE:	Biological activity of human granulocyte colony stimulating factor with a modified C-terminus.
AUTHOR:	Oshima Y; Tojo A; Niho Y; Asano S
CORPORATE SOURCE:	Department of Hematology, University of Tokyo, Tokyo, 108-8639, Japan.
SOURCE:	Biochemical and biophysical research communications, (2000 Jan 27) 267 (3) 924-7. Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200003
ENTRY DATE:	Entered STN: 20000320 Last Updated on STN: 20000320 Entered Medline: 20000309

AB Granulocyte colony-stimulating factor (G-CSF) undergoes receptor-mediated internalization into target cells which are normally restricted to neutrophilic granulocytes and their committed progenitor cells, suggesting that it may be applicable as a myeloid cell-targeting vehicle. To test this notion, we constructed a cDNA encoding a human G-CSF/murine stem cell factor (mSCF) chimeric molecule in a mammalian expression **vector** and transfected NIH3T3 cells with this **plasmid**. The resulting chimeric cytokine consisted of the entire G-CSF sequences fused to Lys148 of mSCF. It can be released from the surface membrane of NIH3T3 transformants through proteolytic cleavage at Ala164 of mSCF. The culture media conditioned by a number of stable transformants, which were confirmed by an enzyme-linked immunosorbent assay (ELISA) to secrete an hG-CSF derivative, were examined for their ability to stimulate CFU-G-derived colony formation as well as the proliferation of G-CSF-dependent NFS-60 cells. The results indicated that this C-terminus modified version of **hG-CSF** is as potent as **recombinant hG-CSF** in both assays.

L20 ANSWER 3 OF 10 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000-0015434 PASCAL

TITLE (IN ENGLISH): Gene expression along the cerebral-spinal axis after regional gene delivery

AUTHOR: MEULI-SIMMEN C.; YONG LIU; YEO T. T.; LIGGITT D.; GUANGHUAN TU; TAO YANG; MEULI M.; KNAUER S.; HEATH T. D.; LONGO F. M.; DEBS R. J.

CORPORATE SOURCE: Division of Reconstructive Surgery, University Hospital, 8091 Zurich, Switzerland; California Pacific Medical Center Research Institute, Stern Building, San Francisco, CA 94115, United States; Department of Neurology, VAMC/UCSF Medical Center, San Francisco, CA 94121, United States; Department of Comparative Medicine, University of Washington School of Medicine, Seattle, WA 98195, United States; Department of Surgery, University Children's Hospital Zurich, 8032 Zurich, Switzerland; School of Pharmacy, University of Wisconsin-Madison, WI 53706, United States

SOURCE: Human gene therapy, (1999), 10(16), 2689-2700, 33 refs.
ISSN: 1043-0342

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-22641, 354000080457010130

AN 2000-0015434 PASCAL

AB We demonstrate here that intracerebroventricular or spinal cord (intrathecal) injection of either **plasmid** DNA alone or cationic liposome: DNA complexes (CLDCs) produces significant levels of expression of both reporter genes and biologically relevant genes in nonparenchymal cells lining both the brain and the spinal cord. Gene expression was identified both within the spinal cord and the brain after intracerebroventricular or intrathecal injection of either CLDCs or **plasmid** DNA alone. Intracerebroventricular or intrathecal injection of CLDCs containing the β-galactosidase (β-Gal) gene produced patchy, widely scattered areas of β-Gal expression. The chloramphenicol acetyltransferase (CAT) reporter gene product reached peak levels between 24 hr and 1 week postinjection, and was still present at significant levels 3 weeks after a single intracerebroventricular or intrathecal injection. Intrathecal injection of the **human granulocyte colony-stimulating** factor (G-CSF) gene produced high levels of **hG-CSF** activity in both the spinal cord and the brain. Intracerebroventricular injection of CLDCs containing the murine nerve growth factor (NGF) gene increased mNGF levels in the hippocampus, a target region for cholinergic neurons in the medial septum, and increased cholinergic neurotransmitter synthetic enzyme choline acetyltransferase (ChAT) activity within the brain, a well-characterized effect of both purified and **recombinant** NGF protein. These findings indicate that intracerebroventricular or intrathecal injection of CLDCs can produce significant levels of

expression of biologically and therapeutically relevant genes within the CNS.

L20 ANSWER 4 OF 10 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:209603 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA13007076809U
TITLE: Over-expression of G-CSF in Escherichia coli and fast purification protocol
AUTHOR(S): Li, Fu-Sheng; Gong, Hui-Yu; Zhao, Bing-Wen; Yu, Cai-Ling; Hou, Bin; Chen, Ai-Jun; Zhang, Zhi-Qing; Hou, Yun-De
CORPORATE SOURCE: State Key Lab. Mol. Virol. Genetic Eng., Inst. Virol. CAPM, Beijing, 100052, Peop. Rep. China.
SOURCE: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao, (1998) Vol. 14, No. 5, pp. 479-484.
CODEN: ZSHXF2. ISSN: 1007-7626.
COUNTRY: CHINA
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1998:756773
LANGUAGE: Chinese
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020509

AB **Recombinant human granulocyte colony stimulating** factor (**rhG-CSF**) is mainly used in neutropenia induced by cytotoxic chemotherapy in clin. practice. After a Chinese human G-CSF cDNA was cloned, the 5' terminal sequence in G-CSF cDNA was thoroughly modified in order to raise the expression level. **Plasmid** pBV220/G-CSF/2-174 was constructed by inserting the modified gene into the pBV220 **vector**. Over 50% of the cellular protein was the **rhG-CSF**. As G-CSF was in inclusion body in E. coli, a simple and stable purification protocol was established, which was very suitable for large-scale purification Firstly, inclusion body was extracted from E. coli, and then, 8 mol/L urea was used to lysis the inclusion body. G-CSF protein was renatured by dilution And the pure G-CSF was recovered by one-step SP-Sepharose FF chromatog. The relative activity of purified G-CSF reached to 3.4 x 108 U/mg protein. A total G-CSF activity from 1 L fermentation was about 1.06 x 1011 U. As demonstrated by N-terminal amino acid sequencing, methionine had thoroughly been removed, so this kind of purified G-CSF may have a low immunogenicity and toxicity.

L20 ANSWER 5 OF 10 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998-0212378 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): High-level expression of a cDNA for human granulocyte colony-stimulating factor in Chinese hamster ovary cells: Effect of 3'-noncoding sequences
AUTHOR: ROTONDARO L.; MAZZANTI L.; MELE A.; ROVERA G.
CORPORATE SOURCE: Department of Biotechnology, Menarini Ricerche S.p.A., 1 Via T. Speri 10, 00040 Pomezia (Roma), Italy; SUDBIOTEC S.r.l., Pomezia (Roma), Italy; The Wistar

Institute, Philadelphia, PA, United States
SOURCE: Molecular biotechnology, (1997), 7(3), 231-240, 22 refs.
ISSN: 1073-6085
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-17423B, 354000075284000030
AN 1998-0212378 PASCAL

AB We compared the production of **recombinant human granulocyte colony-stimulating** factor (**rhG-CSF**) by Chinese hamster ovary (CHO) cells in a transient expression system, using different analogous **vectors** carrying a **human G-CSF**-encoding cDNA under the transcriptional control of the murine cytomegalovirus (CMV) major immediate early promoter. Comparison of two transcription units carrying a human (h)G-CSF cDNA deleted of 3'-untranslated (UTR) sequences containing AT-rich elements (ARE) and using 3'-UTR sequences for processing of transcripts from the SV40 early region or from the rabbit β1 -globin gene showed that use of the sequences from the rabbit β1-globin gene resulted in 7- to 12-fold higher levels of **rhG-CSF** production. Deletion of ARE of **hG-CSF** cDNA resulted in increased **rhG-CSF** synthesis when transcription units using 3'-UTR sequences Ifrom the rabbit β1-globin gene were compared. By contrast, deletion of ARE did not appear to affect **rhG-CSF** production when 3'-UTR sequences from the SV40 early region were used. The most efficient G-CSF transcription unit, fused to a dihydrofolate reductase (DHFR) marker gene and transfected into a CHO cell liñe, yielded initial transfectant CHO cell lines secreting up to 21 µg **rhG-CSF**/1 x 10.sup.6 cells in 24 h. After two rounds of DHFR gene amplification, a cell line was isolated that contains approx 12 copies of the **vector** and produces **rhG-CSF** at a rate of 90 pg/I x 10.sup.6 cells in 24 h.

L20 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 97088290 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8934228
TITLE: Systemic hematological effects of granulocyte colony-stimulating factor produced by irradiated gene-transfected fibroblasts.
AUTHOR: Rosenthal F M; Kulmburg P; Fruh R; Pfeifer C; Veelken H; Mackensen A; Kohler G; Lindemann A; Mertelsmann R
CORPORATE SOURCE: Department of Medicine I (Hematology/Oncology), University Medical Center Freiburg, Germany.
SOURCE: Human gene therapy, (1996 Nov 10) 7 (17) 2147-56.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970313
Last Updated on STN: 19970313

Searcher : Shears 571-272-2528

Entered Medline: 19970303

AB Although long-term expression of therapeutic molecules is necessary for the treatment of permanent deficiencies, short-term expression of therapeutic molecules inducing local or systemic effects is preferable in clinical situations where temporary substitution is the goal. One such clinical setting is the administration of hematopoietic growth factors in cancer chemotherapy-induced myelosuppression. Several **plasmid vectors** containing the human granulocyte colony-stimulating factor (G-CSF) gene under transcriptional control of different regulatory elements were constructed. In vitro production of G-CSF by nonvirally transfected murine fibroblast clones initially increased after lethal irradiation and was detectable for at least 12 days. We also demonstrate that a single injection of irradiated G-CSF-secreting fibroblasts leads to accelerated hematopoietic recovery and mobilization of committed peripheral blood progenitor cells equivalent to that achieved by twice daily s.c. administration of high doses of **recombinant human G-CSF**. Using dicistronic **vectors**, high levels of G-CSF secretion were also obtained in human fibroblasts.

L20 ANSWER 7 OF 10 JAPIO (C) 2004 JPO on STN
ACCESSION NUMBER: 1995-149798 JAPIO
TITLE: NEW POLYPEPTIDE
INVENTOR: KUGA TETSUO; KOMATSU YUKI; MIYAJI HIROMASA; SATO MORIYUKI; OKABE MASAMI; MORIMOTO MAKOTO; ITOU SEIGA; YAMAZAKI MOTOO; YOKOO YOSHIHARU; YAMAGUCHI KAZUO
PATENT ASSIGNEE(S): KYOWA HAKKO KOGYO CO LTD
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 07149798	A	19950613	Heisei	C07K014-535

APPLICATION INFORMATION
STN FORMAT: JP 1994-185787 19940808
ORIGINAL: JP06185787 Heisei
PRIORITY APPLN. INFO.: JP 1986-306799 19861223
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 1995

AN 1995-149798 JAPIO
AB PURPOSE: To obtain an inexpensive new polypeptide having a structure obtained by replacing a part of amino acids of a human granulocyte colony stimulating factor polypeptide with other amino acids or depleting a part of amino acids from the polypeptide, exhibiting high activity and useful for the treatment and prevention of infectious diseases, leukemia, etc. CONSTITUTION: A cDNA coding a **human granulocyte colony stimulating** factor (**hG-CSF**) separated from a normal human peripheral blood macrophage is subjected to site-specific mutation with a restriction enzyme or T4DNA ligase to prepare a DNA fragment coding an amino acid sequence characterized by the replacement of a part of amino acids of the **hG-CSF** polypeptide with other amino acids and/or the depletion of a part of amino acids from the polypeptide. The fragment is linked to a proper **vector** and the obtained **recombinant plasmid** is introduced into a host such as E.coli. The obtained transformant cultured to obtain the objective new polypeptide expressed by fo:

(R<SP>1</SP> is a peptidyl group, etc., of formula II, etc.; R<SP>2</SP> is Cys, Ser, Ala or Thr) and having high **hG-CSF** activity.
COPYRIGHT: (C)1995,JPO

L20 ANSWER 8 OF 10 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:183986 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA12307076436A
TITLE: Expression system for **recombinant human granulocyte-colony stimulating** factor in eukaryotic cell lines
AUTHOR(S): Mele, Antonio; Rotondaro, Luigi
CORPORATE SOURCE: ASSIGNEE: Menarini Ricerche Sud S.p.A.
PATENT INFORMATION: WO 9511982 A1 4 May 1995
SOURCE: (1995) PCT Int. Appl., 31 pp.
CODEN: PIXXD2.
COUNTRY: ITALY
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1995:693426
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020903

AB A process is disclosed for the preparation of **recombinant human granulocyte-colony stimulating** factor (G-CSF) for which is used a **vector** system which comprises at least one of the following elements: (1) a cytomegalovirus (CMV) promoter upstream of a DNA sequence encoding the desired protein, (2) a sequence for processing of RNA transcripts, and (3) a selection and amplification marker sequence. Thus a human G-CSF expression **vector** was prepared in which the 3'-untranslated region of the mRNA containing AUUUA repeated motifs is removed in order to give a high level of protein production The sequence encoding hG-CSF was then cloned into **plasmids** containing, the murine or human cytomegalovirus major immediate-early promoter, and the rabbit β1-globin gene second intron and polyadenylation site. The SV1DHFR transcription unit from com. available **plasmid** pSV2dhfr was inserted to provide a selection marker. High levels of protein were expressed in transfected CHO dhfr- cells. Such **recombinant human G-CSF** can be used for the preparation of pharmaceutical compns. for promoting hematopoiesis, for the augmentation of the defense mechanism against infection, and for the stimulation and hyperprodn. of functionally primed effector cells against malignant diseases.

L20 ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 3
ACCESSION NUMBER: 89227477 EMBASE
DOCUMENT NUMBER: 1989227477
TITLE: Implantation of fibroblasts transfected with human granulocyte colony-stimulating factor cDNA into mice as a model of cytokine-supplement gene therapy.
AUTHOR: Tani K.; Ozawa K.; Ogura H.; Takahashi T.; Akano A.; Watari K.; Matsudaira T.; Tajika K.; Karasuyama H.; Nagata S.; Asano S.; Takaku F.

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Department of Hematology-Oncology, Institute of Medical Science, University of Tokyo, Minato-ku, Tokyo 108, Japan
SOURCE: Blood, (1989) 74/4 (1274-1280).
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A fibroblast-mediated gene delivery method was used for the endogenous expression of **human granulocyte colony-stimulating** factor (G-CSF) as a model for cytokine supplement therapy. **Human G-CSF** cDNA was inserted into the **plasmid** expression **vector** BMGNeo, which contains a partial sequence of bovine papilloma virus and a selectable marker gene. The **recombinant plasmid** (BMGNeo-GCSF) was transfected into NIH/3T3 fibroblasts by the calcium phosphate coprecipitation method, and the stably transformed cells were isolated by G418 selection. An appropriate clone producing a large amount of G-CSF was selected by enzyme immunoassay of the culture supernatants. Southern blot analysis suggested that the BMGNeo-GCSF **plasmid** replicated mainly as an episome, and Nothern blot analysis demonstrated the high expression of **human G-CSF** mRNA in the cells. After the implantation of the G-CSF-producing fibroblasts into nude mice, prominent neutrophilia, about 30-fold the level of normal control, was observed within seven days. Moreover, the number of hematopoietic progenitor cells in spleen remarkably increased for all cell lineages in these mice. To regulate the in vivo expression of G-CSF, we designed a subcutaneous diffusion chamber apparatus that contains the G-CSF-producing fibroblasts. The leukocytosis (neutrophilia) induced in C3H mice after embedding the device quickly disappeared after ethanol treatment of the chamber. Furthermore, reinjection of the G-CSF-producing fibroblasts into the chamber caused a second neutrophilia.

L20 ANSWER 10 OF 10 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:128006 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA10825217269C
TITLE: High-yield expression of modified human granulocyte colony-stimulating factor gene in yeast and Escherichia coli
AUTHOR(S): Cerretti, Douglas Pat; Cosman, David John; Gillis, Stephen; Mochizuki, Diane Yukiko; March, Carl Jack; Price, Virginia Lee; Tushinski, Robert J.; Urdal, David Lloyd
CORPORATE SOURCE: ASSIGNEE: Immunex Corp.
PATENT INFORMATION: EP 243153 A2 28 Oct 1987
SOURCE: (1987) Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1988:217269
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116

Searcher : Shears 571-272-2528

Last Updated on STN: 20021029

AB **Human granulocyte colony-stimulating** factor (**hG-CSF**) derivs. are **recombinantly** produced in high yields in yeast and Escherichia coli hosts. **Plasmid** pBC102.K22 was constructed containing a site-specifically mutagenized hG-CSF gene (having the codon for arginine at position 22 replaced with that for lysine such that a KEX2 protease-sensitive site is eliminated) linked at the 5'-end via a KEX2 recognition site to an α-factor leader sequence and a sequence encoding an antigenic peptide capable of cleavage by bovine enterokinase. Yeast transformed with pBC102.K22 showed 5-fold higher expression than yeast transformed with **vector** containing native hG-CSF protein gene.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 14:19:16 ON 12 OCT 2004)

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L21      136498 S "LEE S"?/AU
L22        1868 S "JEONG K"?/AU
L23         172 S L21 AND L22
L24          21 S (L21 OR L22 OR L23) AND (L8 OR L13)
L25           8 DUP REM L24 (13 DUPLICATES REMOVED)
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L25 ANSWER 1 OF 8 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-598538 [56] WPIDS
DOC. NO. CPI: C2003-162534
TITLE: Producing human granulocyte-colony-stimulating factor (hG-CSF) protein for facilitating secretion and cellular expression comprises using yeast transformed with a vector for protein expression in yeast.
DERWENT CLASS: B04 D16
INVENTOR(S): JUNG, C H; KIM, H C; LEE, G M; **LEE, S J**; **LEE, S W**; LEE, Y P; MUN, D B; JUNG, C; KIM, H; LEE, K; **LEE, S**; LEE, Y; MOON, D
PATENT ASSIGNEE(S): (GLDS) LG LIFE SCI LTD
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003060141	A1	20030724	(200356)*	EN	57

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

KR 2003062854	A	20030728	(200382)		
AU 2003202817	A1	20030730	(200421)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003060141	A1	WO 2003-KR61	20030113
KR 2003062854	A	KR 2002-3289	20020121

AU 2003202817 A1 AU 2003-202817 20030113

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003202817	A1 Based on	WO 2003060141

PRIORITY APPLN. INFO: KR 2002-3289 20020121
AN 2003-598538 [56] WPIDS
AB WO2003060141 A UPAB: 20040107
NOVELTY - Producing human granulocyte-colony-stimulating factor (hG-CSF) protein comprising using yeast transformed with a vector for protein expression in yeast, where the vector comprises a nucleotide sequence encoding hG-CSF protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a synthetic G-CSF gene that comprises a nucleotide sequence of 528 base pairs fully defined in the specification;

(2) a vector for protein expression in yeast (pLES 5), where the vector for protein expression in yeast comprises an inducible yeast promoter, a complex secretory signal, a yeast transcription terminator, selection markers, and a yeast replication origin, therefore enhancing the secretion and extracellular expression of secretory recombinant protein;

(3) a transformed yeast cell (KCTC 10110base pairs), where the vector for hG-CSF expression pLES5 ADH2/GAPDH-hG-CSF is a vector pLES5 ADH2/GAPDH-G01 comprising inu-alpha-proL-KR(EA)3-GCSF; and

(4) producing hG-CSF protein by producing hG-CSF protein using the yeast cells, and then subjecting the resulting protein to aminopeptidase; or producing hG-CSF protein using the yeast cell.

USE - The method is useful for producing hG-CSF protein for facilitating secretion and extracellular expression.

Dwg.0/8

L25 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2001:731048 CAPLUS
DOCUMENT NUMBER: 135:283966
TITLE: Plasmid vectors and **recombinant** production of **human granulocyte colony stimulating** factor (G-CSF) in Escherichia coli
INVENTOR(S): **Lee, Sang-Yup; Jeong, Ki-Jun**
PATENT ASSIGNEE(S): Korea Advanced Institute of Science and Technology, S. Korea
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073081	A1	20011004	WO 2001-KR549	20010331
W: CN, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				

PT, SE, TR
EP 1185675 A1 20020313 EP 2001-922090 20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
US 2003153049 A1 20030814 US 2001-9792 20011213
PRIORITY APPLN. INFO.: KR 2000-17052 A 20000331
WO 2001-KR549 W 20010331

AB The invention relates to construction of plasmid vectors and methods to **recombinant** production of **human granulocyte colony stimulating** factor (G-CSF) in E.coli. The present invention provides a **recombinant** plasmid vector comprising a kanamycin resistance gene, a promoter, an endoxylanase signal sequence, a nucleotide sequence coding for an oligopeptide consisting of 13 amino acids including 6 consecutive histidine residues, and a **human granulocyte colony stimulating** factor (**hG-CSF**) gene. The lower G-C content in N-terminal portion of hG-CSF is created due to inhibitory effect of high G+C content in N-terminal of hG-CSF on transcription and translation. The signal sequence od endoxylanase derived from Bacillus sp. is used for the secretion of hG-CSF protein from E.coli. The present invention also provides an E. coli transformed with the said vector and a process for producing complete hG-CSF protein with high purity from the protein pool secreted by the said microorganism. In accordance with the invention, the hG-CSF protein can be prepared with high purity through rather simple process facilitating secretion of large amount of hG-CSF fusion protein into the periplasm, which does not require complicated processes such as solubilization and subsequent refolding required for isolation of the hG-CSF protein produced in cytoplasm as insol. inclusion bodies by conventional techniques. The hG-CSF protein prepared by this methods can be widely used as an active ingredient in the development of supplementary agents for anticancer therapy.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:99889 CAPLUS
DOCUMENT NUMBER: 136:231300
TITLE: High-level secretory production of **human granulocyte-colony stimulating** factor by fed-batch culture of **recombinant** Escherichia coli
AUTHOR(S): Yim, S. C.; **Jeong, K. J.**; Chang, H. N.; **Lee, S. Y.**
CORPORATE SOURCE: Department of Chemical Engineering and BioProcess Engineering Research Center, Korea Advanced Institute of Science and Technology, Taejon, 305-701, S. Korea
SOURCE: Bioprocess and Biosystems Engineering (2001), 24(4), 249-254
CODEN: BBEIBV; ISSN: 1615-7591
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Secretory production of human granulocyte colony-stimulating factor fusion protein (hG-CSF) by fed-batch culture of Escherichia coli was investigated in both 2.5-L and 30-L fermentors. To develop a fed-batch culture condition that allows efficient production of hG-CSF, different feeding

strategies including pH-stat, exponential and constant feeding were examined Among these, the constant feeding strategy (0.228 g glucose/min) and the exponential feeding that supports a low specific growth rate (μ=0.116 h-1) resulted in the best hG-CSF production Under these conditions, 4.4 g/L of hG-CSF was produced. The effect of induction time on the protein production was also investigated. For the fed-batch cultures carried out with the pH-stat and exponential feeding strategies, induction at higher cell d. (late-exponential phase) resulted in more hG-CSF production compared with induction at lower cell d. (early to mid-exponential phase). The constant feeding strategy that supported best hG-CSF production was applied to the scale-up production of hG-CSF in 30 L of fermentor. The maximum dry cell weight and hG-CSF concentration of 51.7 and 4.2 g/L, resp., was obtained.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:809052 CAPLUS

DOCUMENT NUMBER: 138:50248

TITLE: Pharmacokinetics of **recombinant human granulocyte colony stimulating** factor (rhG-CSE) following intravenous, intramuscular and subcutaneous administration of HM10411 and filgrastim to rats and mice

AUTHOR(S): Kim, In Wha; **Lee, Sang Hoon**; Kim, Young Min; Jung, Sung Youb; Kwon, Se Chang; Chung, Suk Jae; Shim, Chang-Koo

CORPORATE SOURCE: Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea

SOURCE: Yakche Hakhoechi (2001), 31(2), 89-94
CODEN: YAHAEX; ISSN: 0259-2347

PUBLISHER: Korean Society of Pharmaceutics

DOCUMENT TYPE: Journal

LANGUAGE: Korean

AB The pharmacokinetics of **recombinant human granulocyte colony stimulating** factor (rhG-CSF) following i.v., i.m. and s.c. administration of HM10411-lyo and HM10411-liquid (lyophilized and liquid formulations of rhG-CSF, recently under development by Hanmi Pharmaceutical Company) were studied in rats, and compared with that of Filgrastim (conventional formulation of rhG-CSF on market). The plasma concentration of rhG-CSF was quantified using a specific ELISA. The pharmacokinetic parameters of rhG-CSF, after i.v., i.m. and s.c. administration of Filgrastim, HM10411-lyo and HM10411-liquid to rats at a rhG-CSF dose of 10 μg/kg, were almost identical among the three formulations. No dose-dependency was observed in the pharmacokinetic parameters of rhG-CSF following i.v. administration in the dose range of 5.apprx. 100 μg/kg. The rhG-CSF, after i.v. administration of the three prepns. at a dose of 10 μg/kg to rats, was detected at low levels in all of the body tissues with highest tissue/plasma ratio of 0.46.apprx.-0.51 for the kidney at 30 min after the administration. The pharmacokinetics of rhG-CSF, after i.v. administration to mice at a dose

of 10 μg/kg, were comparable among the three formulations. In conclusion, HM10411-lyo and HM10411-liquid exhibited similar pharmacokinetics for rhG-CSF with Filgrastim regardless of animal species. Considering the fact that HM10411 series, contrary to Filgrastim, are proteins lacking a methionine residue, the methionine moiety in rhG-CSF mol. does not appear to influence the pharmacokinetics of the protein significantly.

L25 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:274230 CAPLUS
DOCUMENT NUMBER: 129:23051
TITLE: **Recombinant human granulocyte colony-stimulating** factor (filgrastim) following high-dose chemotherapy and peripheral blood progenitor cell rescue in high-grade non-Hodgkin's lymphoma: clinical benefits at no extra cost
AUTHOR(S): **Lee, S. M.**; Radford, J. A.; Dobson, L.; Huq, T.; Ryder, W. D. J.; Pettengell, R.; Morgenstern, G. R.; Scarffe, J. H.; Crowther, D.
CORPORATE SOURCE: CRC Department of Medical Oncology, Christie Hospital NHS Trust, Manchester, M20 4BX, UK
SOURCE: British Journal of Cancer (1998), 77(8), 1294-1299
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to evaluate the potential clin. and economic benefits of granulocyte colony-stimulating factor (G-CSF, filgrastim) following peripheral blood progenitor cells (PBPC) rescue after high-dose chemotherapy (HDCT), patients aged <60 yr with poor-prognosis, high-grade non-Hodgkin's lymphoma (NHL) were entered into a prospective randomized trial. The patients were randomized to receive either PBPC alone or PBPC plus G-CSF after HDCT with busulphan and cyclophosphamide. G-CSF (300 μg/day) was given from day +5 until recovery of granulocyte count to >1.0 + 109/L for 2 consecutive days. The mean time to achieve a granulocyte count >0.5 + 109/L was shorter with than without G-CSF (9.7 vs. 13.2 days), as was the median duration of hospital stay (12 vs. 15 days). In addition the recovery periods (range 9-12 vs. 11-17 days to achieve a count of 1.0 + 109/L) and hospital stays (range 11-14 vs. 13-22 days) were less variable in patients receiving G-CSF, in whom the values clustered around the median. There were no significant differences between the 2 groups in terms of days of fever, documented episodes of bacteremia, antimicrobial drug usage and platelet/red cell transfusion requirements. Taking into account the costs of total occupied-bed days, drugs, growth factor usage and hematol. support, the mean expenditure per inpatient stay was £6500 (range £5465-£8101) in the G-CSF group compared with £8316 (range £5953-£15,801) in the group not receiving G-CSF, with an observed mean saving of £1816 per patient (or 22% of the total cost) in the G-CSF group. This study suggests that after HDCT and PBPC rescue, the use of G-CSF leads to more rapid hematol. recovery and is associated with a more predictable and shorter hospital stay.
Furthermore, and despite the addnl. costs for G-CSF, these clin. benefits are not translated into increased health care expenditure.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 8 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-528210 [45] WPIDS
TITLE: Method for the purification of **recombinant human granulocyte colony stimulating** element(rhG- CSF) NoAbstract.
DERWENT CLASS: B04 D16
INVENTOR(S): KIM, K; **LEE, S**; KIM, G D; KIM, G W; **LEE, S M**
PATENT ASSIGNEE(S): (GLDS) LG CHEM CO LTD; (GLDS) LG CHEM LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 97070017	A	19971107	(199845)*		
KR 184776	B1	19990401	(200113)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 97070017	A	KR 1996-12597	19960424
KR 184776	B1	KR 1996-12597	19960424

PRIORITY APPLN. INFO: KR 1996-12597 19960424
**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L25 ANSWER 7 OF 8 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-434876 [37] WPIDS
TITLE: Method for purifying **recombinant human granulocyte colony stimulating** factor revealed to be enclosure in yeast.
DERWENT CLASS: B04 D16
INVENTOR(S): KIM, G D; KIM, G W; KIM, S H; **LEE, S M**
PATENT ASSIGNEE(S): (GLDS) LG CHEM CO LTD; (GLDS) LG CHEM LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 97059184	A	19970812	(199837)*		
KR 160934	B1	19981116	(200030)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 97059184	A	KR 1996-649	19960115
KR 160934	B1	KR 1996-649	19960115

PRIORITY APPLN. INFO: KR 1996-649 19960115
**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

Searcher : Shears 571-272-2528

L25 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1995:734128 CAPLUS
DOCUMENT NUMBER: 123:162117
TITLE: High level expression and simple purification of **recombinant human granulocyte colony-stimulating** factor in E. coli
AUTHOR(S): Kang, Soo-Hyung; Na, Kyu-Heum; Park, Jang-Hyeon; Park, Choong-Il; **Lee, Se-Yong**; Lee, Young-Ik
CORPORATE SOURCE: Research Laboratories of Dong-A Pharm. Co., Ltd., Korea University, Seoul, 136-075, S. Korea
SOURCE: Biotechnology Letters (1995), 17(7), 687-92
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Science and Technology Letters
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A human granulocyte colony-stimulating factor (hG-CSF) gene was synthesized and inserted into a trp expression vector for overexpression in E. coli. A strong expression vector was constructed, and a simple purification procedure including in vitro refolding was established. The final productivity of hG-CSF was 500.apprx.600 μg per l culture, and the purified hG-CSF showed the proliferation of neutrophils in vivo assays.

FILE 'HOME' ENTERED AT 14:22:06 ON 12 OCT 2004

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 14:25:07 ON 13 OCT 2004

L1 138204 SEA ABB=ON PLU=ON ("LEE S"? OR "JEONG K"?)/AU
L2 2 SEA ABB=ON PLU=ON L1 AND (RHGCSF OR (RHUG OR RHG)(W)(CSF OR COLONY STIMULAT?))
L3 2 DUP REM L2 (0 DUPLICATES REMOVED)

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:809052 CAPLUS
DOCUMENT NUMBER: 138:50248
TITLE: Pharmacokinetics of recombinant human granulocyte colony stimulating factor (rhG-CSE) following intravenous, intramuscular and subcutaneous administration of HM10411 and filgrastim to rats and mice
AUTHOR(S): Kim, In Wha; **Lee, Sang Hoon**; Kim, Young Min; Jung, Sung Youb; Kwon, Se Chang; Chung, Suk Jae; Shim, Chang-Koo
CORPORATE SOURCE: Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Yakche Hakhoechi (2001), 31(2), 89-94
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB The pharmacokinetics of recombinant human granulocyte colony stimulating factor (**rhG-CSF**) following i.v., i.m. and s.c. administration of HM10411-lyo and HM10411-liquid (lyophilized and liquid formulations of **rhG-CSF**, recently under development by Hanmi Pharmaceutical Company) were studied in rats, and compared with that of Filgrastim (conventional formulation of **rhG-CSF** on market). The plasma concentration of **rhG-CSF** was quantified using a specific ELISA. The pharmacokinetic parameters of **rhG-CSF**, after i.v., i.m. and s.c. administration of Filgrastim, HM10411-lyo and HM10411-liquid to rats at a **rhG-CSF** dose of 10 μg/kg, were almost identical among the three formulations. No dose-dependency was observed in the pharmacokinetic parameters of **rhG-CSF** following i.v. administration in the dose range of 5.apprx. 100 μg/kg. The **rhG-CSF**, after i.v. administration of the three prepns. at a dose of 10 μg/kg to rats, was detected at low levels in all of the body tissues with highest tissue/plasma ratio of 0.46.apprx.-0.51 for the kidney at 30 min after the administration. The pharmacokinetics of **rhG-CSF**, after i.v. administration to mice at a dose of 10 μg/kg, were comparable among the three formulations. In conclusion, HM10411-lyo and HM10411-liquid exhibited similar pharmacokinetics for **rhG-CSF** with Filgrastim regardless of animal species. Considering the fact that HM10411 series, contrary to Filgrastim, are proteins lacking a methionine residue, the methionine moiety in **rhG-CSF** mol. does not appear to influence the pharmacokinetics of the protein significantly.

L3 ANSWER 2 OF 2 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-528210 [45] WPIDS
TITLE: Method for the purification of recombinant human

granulocyte colony stimulating element(**rhG-CSF**) NoAbstract.
DERWENT CLASS: B04 D16
INVENTOR(S): KIM, K; **LEE, S**; KIM, G D; KIM, G W; **LEE, S M**
PATENT ASSIGNEE(S): (GLDS) LG CHEM CO LTD; (GLDS) LG CHEM LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 97070017	A	19971107	(199845)*		
KR 184776	B1	19990401	(200113)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 97070017	A	KR 1996-12597	19960424
KR 184776	B1	KR 1996-12597	19960424

PRIORITY APPLN. INFO: KR 1996-12597 19960424
**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

FILE 'HOME' ENTERED AT 14:26:57 ON 13 OCT 2004

Devi, S.
10/009792

12oct04 13:21:21 User219783 Session D2050.2

SYSTEM:OS - DIALOG OneSearch
File 65:Inside Conferences 1993-2004/Oct W2
(c) 2004 BLDSC all rts. reserv.
File 440:Current Contents Search(R) 1990-2004/Oct 12
(c) 2004 Inst for Sci Info
File 348:EUROPEAN PATENTS 1978-2004/Oct W01
(c) 2004 European Patent Office
File 357:Derwent Biotech Res. _1982-2004/Oct W3
(c) 2004 Thomson Derwent & ISI
File 113:European R&D Database 1997
(c)1997 Reed-Elsevier(UK)Ltd All rts reserv
*File 113: This file is closed (no updates)

Set Items Description
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-key terms

Set Items Description
S1 1764 HGCSF OR (HG OR HUMAN(W)GRANULOCYT?)(W)(CSF OR COLONY(W)ST-IMULAT?)
S2 1980 HUMAN(W)(GCSF OR (G OR GRANULOCYT?)(W)(CSF OR COLONY(W)STI-MULAT?) OR RHGCSF OR (RHUG OR RHG)(W)(CSF OR COLONY(W)STIMULA-T?))

S10 1543 (S1 OR S2)(10N)RECOMBINAN?

S23 46 S10 AND (PLASMID? ?(5N)VECTOR? ?)
S24 46 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

24/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2004 Inst for Sci Info. All rts. reserv.

08111379 References: 39
TITLE: Systemic hematological effects of granulocyte colony-stimulating factor produced by irradiated gene-transfected fibroblasts
AUTHOR(S): Rosenthal FM (REPRINT); Kulmburg P; Fruh R; Pfeifer C; Veelken H ; Mackensen A; Kohler G; Lindemann A; Mertelsmann R
CORPORATE SOURCE: UNIV FREIBURG,MED CTR, DEPT INTERNAL MED 1, HUGSTETTER STR 55/D-79106 FREIBURG//GERMANY/ (REPRINT); UNIV FREIBURG,MED CTR, DEPT MED HEMATOL ONCOL 1/D-79106 FREIBURG//GERMANY/; UNIV FREIBURG,MED CTR, DEPT SURG/D-79106 FREIBURG//GERMANY/; UNIV FREIBURG,MED CTR, DEPT PATHOL/D-79106 FREIBURG//GERMANY/
PUBLICATION TYPE: JOURNAL
PUBLICATION: HUMAN GENE THERAPY, 1996, V7, N17 (NOV 10), P2147-2156
GENUINE ARTICLE#: WD328
PUBLISHER: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538
ISSN: 1043-0342
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Although long-term expression of therapeutic molecules is necessary for the treatment of permanent deficiencies, short-term expression of therapeutic molecules inducing local or systemic effects is preferable in clinical situations where temporary substitution is the goal. One such clinical setting is the administration of hematopoietic growth

factors in cancer chemotherapy-induced myelosuppression. Several **plasmid vectors** containing the human granulocyte colony-stimulating factor (G-CSF) gene under transcriptional control of different regulatory elements were constructed. In vitro production of G-CSF by nonvirally transfected murine fibroblast clones initially increased after lethal irradiation and was detectable for at least 12 days. We also demonstrate that a single injection of irradiated G-CSF-secreting fibroblasts leads to accelerated hematopoietic recovery and mobilization of committed peripheral blood progenitor cells equivalent to that achieved by twice daily s.c. administration of high doses of **recombinant human G-CSF**. Using dicistronic vectors, high levels of G-CSF secretion were also obtained in human fibroblasts.

24/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08018324 References: 26
TITLE: Expression of **recombinant human granulocyte colony-stimulating** factor in CHO dbfr(-) cells: New insights into the in vitro amplification expression system
AUTHOR(S): Monaco L (REPRINT); Tagliabue R; Giovanazzi S; Bragonzi A; Soria MR
CORPORATE SOURCE: SAN RAFFAELE SCI INST,DIBIT, BIOTECHNOL UNIT, VIA OLGETTINA 58/I-20132 MILAN//ITALY/ (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: GENE, 1996, V180, N1-2 (NOV 21), P145-150
GENUINE ARTICLE#: VY054
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
ISSN: 0378-1119
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The in vitro amplification method for heterologous gene expression in mammalian cells is based on the stable transfection of cells with long, linear DNA molecules having several copies of complete expression units, coding for the gene of interest, linked to one terminal unit, coding for the selectable marker. DNA concatenamers containing additional expression units can also be prepared: we exploited this feature by co-polymerizing expression units coding for granulocyte colony-stimulating factor (G-CSF) with cassettes for dihydrofolate reductase (DHFR) and for neomycin (Nm) resistance, as selectable markers. We were thus able to obtain high level production of G-CSF in chinese hamster ovary (CHO) dhfr(-) cells by combining in vitro amplification to just one step of in vivo amplification. This approach required a considerably shorter time than the classical, stepwise amplification by methotrexate.

24/3,AB/3 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01789829
Modulators of the megalin-mediated uptake of radiotherapeutics and/or radiodiagnostics into kidney cells and their use in therapy and

diagnostics
Modulatoren der Megalin-vermittelten Aufnahme von Radiotherapeutika und/oder Radiodiagnostica in die Nierenzellen und ihre Verwendung in Therapie und Diagnose
Modulateurs de la capture de composes radiotherapeutiques et/ou radiodiagnostiques par l'intermediaire de la megalin des cellules renales et leur utilisation en therapie et diagnostique
PATENT ASSIGNEE:
Schering AG, (4316991), Mullerstrasse 170-178, 13342 Berlin, (DE), (Applicant designated States: all)
INVENTOR:
Brautigam, Matthias, Droysenstrasse 8, 10629 Berlin, (DE)
Zerhusen, Sandra, Erasmusstrasse 17, 10553 Berlin, (DE)
LEGAL REPRESENTATIVE:
Krauss, Jan (124271), Forrester & Boehmert, Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1462119 A1 040929 (Basic)
APPLICATION (CC, No, Date): EP 2003006592 030324;
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IT; LI; LU; MC; NL; PT; RO; SE; SI; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK
INTERNATIONAL PATENT CLASS: A61K-051/10; A61K-049/00; G01N-033/566

ABSTRACT EP 1462119 A1
The present invention broadly relates to the treatment, diagnosis, and prophylactic prevention of cancer disease. More specifically, the present invention relates to methods and compositions for preventing the endocytosis of radiopharmaceutics into cells of the kidney and the subsequent radioinduced damaging of the kidney catabolism by blocking or interfering with the association or binding of radiotherapeutics and/or radiodiagnostics to the receptor megalin, a member of the LDL-receptor family. In another aspect of the present invention, the expression of megalin is altered, in order to prevent the endocytosis and cellular internalisation of radiopharmaceutics into cells of the kidney.
ABSTRACT WORD COUNT: 98
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200440	1731
SPEC A	(English)	200440	37804
Total word count - document A			39535
Total word count - document B			0
Total word count - documents A + B			39535

24/3,AB/4 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01746624
Ligands for flt3 receptors
Liganden fur die flt3 Rezeptoren
Ligands pour les recepteurs flt3

PATENT ASSIGNEE:
IMMUNEX CORPORATION, (485033), 51 University Street, Seattle Washington 98101, (US), (Applicant designated States: all)
INVENTOR:
Lyman, Stewart D., 1836 53rd Street, Seattle Washington 98103, (US)
Beckmann, M. Patricia, 5454 Ragan Lane, Poulsbo Washington 98370, (US)
LEGAL REPRESENTATIVE:
Bassil, Nicholas Charles et al (91231), Kilburn & Strode 20 Red Lion Street, London WC1R 4PJ, (GB)
PATENT (CC, No, Kind, Date): EP 1428834 A1 040616 (Basic)
APPLICATION (CC, No, Date): EP 2003078708 940519;
PRIORITY (CC, No, Date): US 68394 930524; US 106463 930812; US 111758 930825; US 162407 931203; US 209502 940307; US 243545 940511
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 627487 (EP 94303575)
INTERNATIONAL PATENT CLASS: C07K-014/475; C07K-014/71; C07K-016/22; A61K-038/18; C12P-021/08; C12N-015/12

ABSTRACT EP 1428834 A1
Ligands for flt3 receptors capable of transducing self-renewal signals to regulate the growth, proliferation or differentiation of progenitor cells and stem cells are disclosed. The invention is directed to flt3-L as an isolated protein, the DNA encoding the flt3-L, host cells transfected with cDNAs encoding flt3-L, compositions comprising flt3-L, methods of improving gene transfer to a mammal using flt3-L, and methods of improving transplantations using flt3-L. Flt3 -L finds use in treating patients with anemia, AIDS and various cancers.
ABSTRACT WORD COUNT: 80

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200425	717
SPEC A	(English)	200425	15595
Total word count - document A			16312
Total word count - document B			0
Total word count - documents A + B			16312

24/3,AB/5 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01674697
Thrombopoietin compositions for increasing circulating platelets
Thrombopoietinzusammensetzungen zur Verhohung von zirkulierenden Plattchen
Compositions de thrombopoietine pour l'augmentation de plaquettes circulantes
PATENT ASSIGNEE:
BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM, (266341), Office of the General Counsel, 201 West 7th Street, Austin, Texas 78701, (US), (Applicant designated States: all)
INVENTOR:
Vadhan-Raj, Saroj, 21 Harbor View Drive, Sugarland, TX 77479, (US)

LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance et al (61534), Forrester & Boehmert Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1374890 A2 040102 (Basic)
EP 1374890 A3 040825
APPLICATION (CC, No, Date): EP 2003021505 000128;
PRIORITY (CC, No, Date): US 239442 990128; US 244370 990204
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 1146895 (EP 2000913278)
INTERNATIONAL PATENT CLASS: A61K-038/19; A61K-035/12; A61P-007/00

ABSTRACT EP 1374890 A2
The present invention relates generally to the fields of platelet production in a patient and cryopreservation of platelets isolated from a patient. More particularly, it concerns transfusion of autologous of allorgeneic cryopreserved platelets into a patient to prevent or manage thrombocytopenia.
ABSTRACT WORD COUNT: 42
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200401	1117
SPEC A	(English)	200401	55214
Total word count - document A			56331
Total word count - document B			0
Total word count - documents A + B			56331

24/3,AB/6 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01444315
G-CSF analog compositions and methods
Zusammenstellungen von G-CSF Analoge und Methode
Compositions d'analogues de G-CSF et methodes
PATENT ASSIGNEE:
AMGEN INC., (923238), Amgen Center, One Amgen Center Drive, Thousand Oaks, CA 91320-1789, (US), (Applicant designated States: all)
INVENTOR:
Osslund, Timothy, 475 Vista Montana, Camarillo, California 93010, (US)
LEGAL REPRESENTATIVE:
Brown, John David (28811), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1233065 A1 020821 (Basic)
APPLICATION (CC, No, Date): EP 2001128744 940127;
PRIORITY (CC, No, Date): US 10099 930128
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 965638 (EP 99112115)

EP 612846 (EP 94101207)
INTERNATIONAL PATENT CLASS: C12N-015/27; C07K-014/535; A61K-038/19; C07K-019/00; C07K-001/00; C12N-015/62

ABSTRACT EP 1233065 A1
Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.
ABSTRACT WORD COUNT: 90
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200234	618
SPEC A	(English)	200234	17703
Total word count - document A			18321
Total word count - document B			0
Total word count - documents A + B			18321

24/3,AB/7 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01406846
METHOD FOR SCREENING LIGAND HAVING BIOLOGICAL ACTIVITY
VERFAHREN ZUM SCREENEN EINES LIGANDEN MIT BIOLOGISCHER AKTIVITAT
METHODE DE CRIBLAGE D'UN LIGAND DOTE D'UNE ACTIVITE BIOLOGIQUE
PATENT ASSIGNEE:
CHUGAI SEIYAKU KABUSHIKI KAISHA, (207666), 5-1, Ukima 5-chome, Kita-ku, Tokyo, 115-8543, (JP), (Applicant designated States: all)
INVENTOR:
YABUTA, Naohiro, c/o CHUGAI SEIYAKU KABUSHIKI K., 1-135, Komakado, Gotenba-shi, Shizuoka 412-8513, (JP)
ADACHI, Hideki, c/o CHUGAI SEIYAKU KABUSHIKI K., 1-135, Komakado, Gotenba-shi, Shizuoka 412-8513, (JP)
SHIMONAKA, Yasushi, c/o CHUGAI SEIYAKU KABUSHIKI K, 1-135, Komakado, Gotenba-shi, Shizuoka 412-8513, (JP)
HATTORI, Kunihiro, c/o CHUGAI SEIYAKU KABUSHIKI K., 1-135, Komakado, Gotenba-shi, Shizuoka 412-8513, (JP)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1304573 A1 030423 (Basic)
WO 2002006838 020124
APPLICATION (CC, No, Date): EP 2001950013 010717; WO 2001JP6170 010717
PRIORITY (CC, No, Date): JP 2000221070 000717; JP 2001159032 010528
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: G01N-033/566; G01N-033/50; G01N-033/15; C12N-005/00; C12N-015/00

ABSTRACT EP 1304573 A1
In the case when there are two objective biological activities, and the aim is to isolate a compound having at least one biological activity, the present inventors developed an assay method wherein a common detection marker is utilized for separately detecting the presence or absence of each of the biological activities. The present inventors discovered that a compound having at least one of two or more distinct biological activities can be efficiently and conveniently detected by simultaneously assaying at least one test sample or more by the above-mentioned method. Furthermore, for a test sample that proved to be positive by the detection method, they found that it is possible to efficiently and conveniently screen for a test sample having an objective specific biological activity by combining with a method wherein an individual activity of a test sample can be detected to specify the biological activity.
ABSTRACT WORD COUNT: 146
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200317	1113
SPEC A	(English)	200317	16737
Total word count - document A			17850
Total word count - document B			0
Total word count - documents A + B			17850

24/3,AB/8 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01402621
Production of pluripotent granulocyte colony-stimulating factor
Produktion des pluripotenten Granulozyten-Koloniestimulierungsfaktors
Production du facteur pluripotent de stimulation de colonies de granulocytes
PATENT ASSIGNEE:
Kirin-Amgen, Inc., (650490), 1900 Oak Terrace Lane, Thousand Oaks California 91320, (US), (Applicant designated States: all)
INVENTOR:
Souza, Lawrence M., 417 Camino de Celeste, Thousand Oaks, CA 91360, (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1186663 A1 020313 (Basic)
APPLICATION (CC, No, Date): EP 2001118552 860822;
PRIORITY (CC, No, Date): US 768959 850823; US 835548 860303
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 396158 (EP 90111660)

EP 237545 (EP 86905530)
INTERNATIONAL PATENT CLASS: C12N-015/27; C07K-014/535; A61K-038/19; C12N-001/21; C12N-005/10

ABSTRACT EP 1186663 A1
Disclosed are novel polypeptides possessing part or all of the primary structural conformation and one or more of the biological properties of a mammalian (e.g., human) pluripotent granulocyte colony-stimulating factor ("hpG-CSF") which are characterized in preferred forms by being the product of procaryotic or eucaryotic host expression of an exogenous DNA sequence. Sequences coding for part or all of the sequence of amino acid residues of hpG-CSF or for analogs thereof may be incorporated into autonomously replicating **plasmid** or viral **vectors** employed to transform or transfect suitable procaryotic or eucaryotic host cells such as bacteria, yeast or vertebrate cells in culture. Products of expression of the DNA sequences display, e.g., the physical and immunological properties and in vitro biological activities of isolates of hpG-CSF derived from natural sources. Disclosed also are chemically synthesized polypeptides sharing the biochemical and immunological properties of hpG-CSF.
ABSTRACT WORD COUNT: 143
NOTE:
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200211	1661
SPEC A	(English)	200211	11832
Total word count - document A			13493
Total word count - document B			0
Total word count - documents A + B			13493

24/3,AB/9 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01378175
USE OF CXCR4 ANTAGONISTS FOR TREATING AUTOIMMUNE DISEASES AND CANCER
VERWENDUNG VON CXCR4 ANTAGONISTEN ZUR BEHANDLUNG VON KREBS UND AUTOIMMUNKRANKHEITEN
UTILISATION D'ANTAGONISTES DU CXCR4 POUR TRAITER LES MALADIES AUTOIMMUNES ET LE CANCER
PATENT ASSIGNEE:
THE UNIVERSITY OF BRITISH COLUMBIA, (917325), IRC Building, Room 331, 2194 Health Sciences Mall, Vancouver, British Columbia V6T 1Z3, (CA), (Proprietor designated states: all)
Chemokine Therapeutics Corporation, (3908512), 2386 East Mall, Unit 208, Vancouver, British Columbia V6T 1Z4, (CA), (Proprietor designated states: all)
INVENTOR:
TUDAN, Christopher, R., 330 Cochrane Drive, Markham, Ontario, L3R 8E4, (CA)
MERZOUK, Ahmed, 9071 No. 5 Road, 112, Richmond, British Columbia V7A 4E1, (CA)
ARAB, Lakhdar, 301-975 West 13th avenue, Vancouver, British Columbia V5Z

1P4, (CA)
SAXENA, Geeta, 110-2875 Osoyoos Crescent, Vancouver, British Columbia V6T 2G3, (CA)
EAVES, Connie, J., 2705 West 31st Avenue, Vancouver, British Columbia V6L 1Z9, (CA)
CASHMAN, Johanne, 6070 Blenheim Street, Vancouver, British Columbia V6N 1R1, (CA)
CLARK-LEWIS, Ian, 2875 Osoyoos Crescent, 409, Vancouver, British Columbia V6T 1X5, (CA)
SALARI, Hassan, 927 Pacific Drive, Delta, British Columbia V4M 2K2, (CA)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance (61531), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1286684 A2 030305 (Basic)
EP 1286684 B1 040428
WO 2001085196 011115
APPLICATION (CC, No, Date): EP 2001931279 010509; WO 2001CA659 010509
PRIORITY (CC, No, Date): CA 2305787 000509; US 205467 P 000519
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003027506)
INTERNATIONAL PATENT CLASS: A61K-038/10; A61K-038/16; A61K-038/19; A61P-035/00; A61P-037/06
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200418	212
CLAIMS B	(German)	200418	198
CLAIMS B	(French)	200418	224
SPEC B	(English)	200418	14706
Total word count - document A			0
Total word count - document B			15340
Total word count - documents A + B			15340

24/3,AB/10 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01366345
CXCR4 AGONIST TREATMENT OF HEMATOPOIETIC CELLS
BEHANDLUNG VON HEMATOPOIETISCHEN ZELLEN MIT CXCR4 AGONISTEN
TRAITEMENT DE CELLULES HEMATOPOIETIQUES UTILISANT DES AGONISTES DE CXCR4
PATENT ASSIGNEE:
The University of British Columbia, (3412849), University Industry Liaison Office, IRC Building, Room 331, Health Science Mall, Vancouver, British Columbia V6T 1Z3, (CA), (Proprietor designated states: all)
Chemokine Therapeutics Corporation, (3908513), 2211 Wesbrook Mall, Unit F238, Vancouver, British Columbia V6T 2B5, (CA), (Proprietor designated states: all)
INVENTOR:
SALARI, Hassan, 927 Pacific Drive, Delta, British Columbia V4M 2K2, (CA)

MERZOUK, Ahmed, 9071 No. 5 Road, 112, Richmond, British Columbia V7A 4E1 , (CA)
ARAB, Lakhdar, #301-975 West 13th Avenue, Vancouver, British Columbia V5Z 1P4, (CA)
TUDAN, Christopher, R., Cytochroma Inc, 330 Cochrane Drive, Markham, Ontario, L3R 8E4, (CA)
SAXENA, Geeta, 110-2875 Osoyoos Crescent, Vancouver, British Columbia V6T 2G3, (CA)
EAVES, Connie, J., 2705 West, 31st Avenue, Vancouver, British Columbia V6L 1Z9, (CA)
CASHMAN, Johanne, 6070 Blenheim Street, Vancouver, British Columbia V6N 1R1, (CA)
CLARK-LEWIS, Ian, deceased ##, ##, (CA)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance (61531), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1276493 A2 030122 (Basic)
EP 1276493 B1 040929
WO 2001076615 011018
APPLICATION (CC, No, Date): EP 2001925259 010412; WO 2001CA540 010412
PRIORITY (CC, No, Date): CA 2305036 000412; US 232425 P 000914; CA 2335109 010223
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-038/10; C07K-014/52
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200440	825
CLAIMS B	(German)	200440	770
CLAIMS B	(French)	200440	872
SPEC B	(English)	200440	15406
Total word count - document A			0
Total word count - document B			17873
Total word count - documents A + B			17873

24/3,AB/11 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01195513
THROMBOPOIETIN COMPOSITIONS FOR INCREASING CIRCULATING PLATELETS
ERHOHUNG VON ZIRKULIERENDEN PLATTCHEN MIT THROMBOPOIETINZUSAMMENSETZUNGEN
AUGMENTATION DE PLAQUETTES CIRCULANTES AVEC DES COMPOSITIONS DE THROMBOPOIETINE
PATENT ASSIGNEE:
BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM, (266341), Office of General Council, 201 West 7th Street, Austin, Texas 78701, (US), (Proprietor designated states: all)
INVENTOR:
VADHAN-RAJ, Saroj, 21 Harbor View Drive, Sugarland, TX 77479, (US)

LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance et al (61531), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1146895 A2 011024 (Basic)
EP 1146895 B1 031112
WO 2000044398 000803
APPLICATION (CC, No, Date): EP 2000913278 000128; WO 2000US2173 000128
PRIORITY (CC, No, Date): US 239442 990128; US 244370 990204
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003021505)
INTERNATIONAL PATENT CLASS: A61K-038/19; A61K-035/12; A61P-007/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200346	801
CLAIMS B	(German)	200346	727
CLAIMS B	(French)	200346	844
SPEC B	(English)	200346	54085
Total word count - document A			0
Total word count - document B			56457
Total word count - documents A + B			56457

24/3,AB/12 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01112809
G-CSF analog compositions and methods
G-G-CSF Analoge und Verfahren zu ihrer Herstellung
Analogues de G-CSF et methodes pour les obtenir
PATENT ASSIGNEE:
Amgen Inc.,, (923239), One Amgen Center Drive, Thousand Oaks, California 91320-1799, (US), (Applicant designated States: all)
INVENTOR:
Osslund, Timothy, 475 Vista Montana, Camarillo, California 93010, (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 974655 A2 000126 (Basic)
EP 974655 A3 011024
APPLICATION (CC, No, Date): EP 99113571 940127;
PRIORITY (CC, No, Date): US 10099 930128
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 612846 (EP 94101207)
INTERNATIONAL PATENT CLASS: C12N-015/27; C07K-014/535; C07K-001/00

ABSTRACT EP 974655 A2
Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions.

In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.
ABSTRACT WORD COUNT: 90
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200004	1563
SPEC A	(English)	200004	17721
Total word count - document A			19284
Total word count - document B			0
Total word count - documents A + B			19284

24/3,AB/13 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01101395
G-CSF analog compositions and methods
G-CSF Analoge und Verfahren zu ihrer Herstellung
Analogues de G-CSF et methodes pour les obtenir
PATENT ASSIGNEE:
AMGEN INC., (923238), Amgen Center, One Amgen Center Drive, Thousand Oaks, CA 91320-1789, (US), (Applicant designated States: all)
INVENTOR:
Osslund, Timothy, 475 Vista Montana, Camarillo, CA 93010, (US)
LEGAL REPRESENTATIVE:
Brown, John David (28811), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 965638 A2 991222 (Basic)
EP 965638 A3 000223
APPLICATION (CC, No, Date): EP 99112115 940127;
PRIORITY (CC, No, Date): US 10099 930128
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 612846 (EP 94101207)
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2001128744)
INTERNATIONAL PATENT CLASS: C12N-015/27; C07K-014/535; G06F-017/50

ABSTRACT EP 965638 A2
Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof.

In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.
ABSTRACT WORD COUNT: 90
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	199951	31
SPEC A	(English)	199951	17731
Total word count - document A			17762
Total word count - document B			0
Total word count - documents A + B			17762

24/3,AB/14 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00983560
G-CSF analog compositions and methods
G-CSF Analoge und Verfahren zu ihrer Herstellung
Analogues de G-CSF et methodes pour les obtenir
PATENT ASSIGNEE:
AMGEN INC., (923238), Amgen Center, One Amgen Center Drive, Thousand Oaks, CA 91320-1789, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Osslund, Thimothy, 475 Vista Montana, Camarillo, California 93010, (US)
LEGAL REPRESENTATIVE:
Brown, John David (28811), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 890640 A2 990113 (Basic)
EP 890640 A3 990324
APPLICATION (CC, No, Date): EP 98113221 940127;
PRIORITY (CC, No, Date): US 10099 930128
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 612846 (EP 941012072)
INTERNATIONAL PATENT CLASS: C12N-015/27; C07K-014/535; A61K-038/19; C07K-019/00; C07K-001/00; C12N-015/62;

ABSTRACT EP 890640 A2
Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.
ABSTRACT WORD COUNT: 90

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9902	171
SPEC A	(English)	9902	15731
Total word count - document A			15902
Total word count - document B			0
Total word count - documents A + B			15902

24/3,AB/15 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00926753
DEFORMYLATION OF f-MET PEPTIDES IN BACTERIAL EXPRESSION SYSTEMS
DEFORMYLIERUNG VON f-MET PEPTIDEN IN BAKTERIEN EXPRESSIONSSYSTEMEN
DEFORMYLATION DE PEPTIDES f-MET DANS DES SYSTEMES D'EXPRESSION BACTERIENS
PATENT ASSIGNEE:
Monsanto Technology LLC, (3342690), 800 North Lindbergh Boulevard, St. Louis, Missouri 63167, (US), (Proprietor designated states: all)
INVENTOR:
BOGOSIAN, Gregg, 262 Village Mead, Ballwin, MO 63021, (US)
LEGAL REPRESENTATIVE:
Bosch, Henry A. et al (58888), Monsanto Services International S.A., Patent Department, Avenue de Tervuren 270/272, Letter Box No. 21, 1150 Brussels, (BE)
PATENT (CC, No, Kind, Date): EP 917580 A1 990526 (Basic)
EP 917580 B1 031217
WO 98003664 980129
APPLICATION (CC, No, Date): EP 97933523 970717; WO 97US12458 970717
PRIORITY (CC, No, Date): US 22687 P 960719
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/55; C12N-015/18; C07K-014/61; C12N-001/21; C12N-001/21; C12R-1:19
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200351	1576
CLAIMS B	(German)	200351	1431
CLAIMS B	(French)	200351	1837
SPEC B	(English)	200351	6263
Total word count - document A			0
Total word count - document B			11107
Total word count - documents A + B			11107

24/3,AB/16 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00767636

Compositions and method for treating or preventing infections in animals
Zusammensetzungen und Verfahren zur Behandlung oder Vorbeugung von Infektionen bei Tieren
Compositions et methode de traitement ou de prevention des infections chez les animaux
PATENT ASSIGNEE:
AMGEN INC., (923231), 1840 Dehavilland Drive, Thousand Oaks California 91320 -1789, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Boone, Thomas C., 3913 Elkwood, Newbury Park, California 91320, (US)
Miller, Allan L., 2111 Balmain Way, Glendale, California 91206, (US)
Andresen, Jeffrey W., 6020 N.Heatherton Drive, Somis, California 93066, (US)
LEGAL REPRESENTATIVE:
Brown, John David (28811), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 719860 A1 960703 (Basic)
APPLICATION (CC, No, Date): EP 95119327 890512;
PRIORITY (CC, No, Date): US 193857 880513; US 348011 890509
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 347041 (EP 893048538)
INTERNATIONAL PATENT CLASS: C12N-015/24; C07K-014/535; C07K-001/18; C12P-021/02; A61K-038/19;

ABSTRACT EP 719860 A1
Compositions and method for treating or preventing bacterial infections such as mastitis in animals, particularly bovine animals, which comprises administering an effective amount of granulocyte colony stimulating factor (G-CSF), are disclosed. The G-CSF may be naturally derived, or alternatively, the G-CSF and genetically engineered variants of G-CSF may be the expression products of genetically engineered prokaryotic or eukaryotic host cells.
ABSTRACT WORD COUNT: 75

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	172
SPEC A	(English)	EPAB96	14606
Total word count - document A			14778
Total word count - document B			0
Total word count - documents A + B			14778

24/3,AB/17 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00677200
Compositions comprising G-CSF for treating or preventing infections in canine and feline animals.
Zusammensetzungen, die G-CSF enthalten zur Behandlung der Vorbeugung von Infektionen bei Hunden und Katzen Tieren.
Compositions contenant du G-CSF pour le traitement ou pour la prevention

d'infections chez des animaux canins et felins.
PATENT ASSIGNEE:
AMGEN INC., (923231), 1840 Dehavilland Drive, Thousand Oaks California 91320 -1789, (US), (applicant designated states: AT;BE;CH;DE;DK;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Boone, Thomas C., 3010 Deer Valley Avenue, Newbury Park, California 91320 , (US)
Miller, Allan L., 2111 Balmain Way, Glendale, California 91206, (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, D-80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 648501 A1 950419 (Basic)
APPLICATION (CC, No, Date): EP 94116853 900927;
PRIORITY (CC, No, Date): US 420038 891010
DESIGNATED STATES: AT; BE; CH; DE; DK; FR; GB; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 447523 (EP 909148397)
INTERNATIONAL PATENT CLASS: A61K-038/19;

ABSTRACT EP 648501 A1
Compositions and methods for treating or preventing infections in canine or feline animals which comprises administering an effective amount of granulocyte colony stimulating factor (G-CSF), are disclosed. The G-CSF may be naturally derived, or alternatively, the G-CSF and genetically engineered variants of G-CSF may be the expression products of genetically engineered prokaryotic or eukaryotic host cells.
ABSTRACT WORD COUNT: 58

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	249
SPEC A	(English)	EPAB95	6995
Total word count - document A			7244
Total word count - document B			0
Total word count - documents A + B			7244

24/3,AB/18 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00674788
A process for producing a substance
Verfahren zur Herstellung einer Substanz
Procede pour la production d'une substance
PATENT ASSIGNEE:
KYOWA HAKKO KOGYO CO., LTD., (229067), 6-1, Ohtemachi 1-chome, Chiyoda-ku, Tokyo 100-8185, (JP), (Proprietor designated states: all)
INVENTOR:
Oda, Hideki, 9-11, Nakamachi 3-chome, Machida-shi, Tokyo, (JP)
Nakagawa, Satoshi, 9-9, Nakamachi 3-chome, Machida-shi, Tokyo, (JP)
Anazawa, Hideharu, 19-18, Minamioizumi 4-chome, Nerima-ku, Tokyo, (JP)
LEGAL REPRESENTATIVE:
Woods, Geoffrey Corlett et al (48721), J.A. KEMP & CO. Gray's Inn 14

South Square, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 646645 A2 950405 (Basic)
EP 646645 A3 950802
EP 646645 B1 020130
APPLICATION (CC, No, Date): EP 94307133 940929;
PRIORITY (CC, No, Date): JP 93246478 931001
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/70; C12R-001/19; C12N-015/01

ABSTRACT EP 646645 A2
The invention relates to a process for producing a desired substance by culturing a transformant in a medium until the desired substance is accumulated in the culture and then recovering the desired substance, said transformant being obtained by transforming an acetic acid-resistant microorganism of the genus Escherichia with a recombinant plasmid carrying a gene involved in production of the desired substance. The present process enables cells to be cultured easily at high density while the desired substance can be efficiently produced.
ABSTRACT WORD COUNT: 83

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	161
CLAIMS B	(English)	200205	303
CLAIMS B	(German)	200205	313
CLAIMS B	(French)	200205	351
SPEC A	(English)	EPAB95	4629
SPEC B	(English)	200205	4582
Total word count - document A			4791
Total word count - document B			5549
Total word count - documents A + B			10340

24/3,AB/19 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00651577
Ligands for FLT3 receptors.
Ligante fur die FLT3 Rezeptoren.
Liants pour les recepteurs FLT3.
PATENT ASSIGNEE:
IMMUNEX CORPORATION, (485033), 51 University Street, Seattle Washington 98101, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Lyman, Stewart D., 312 N. 4th Street, Seattle, Washington 98115, (US)
Beckmann, M. Patricia, 5454 Ragan Lane, Poulsbo, Washington 98370, (US)
LEGAL REPRESENTATIVE:
Cornish, Kristina Victoria Joy (79701), Kilburn & Strode, 20 Red Lion Street, London WC1R 4PJ, (GB)
PATENT (CC, No, Kind, Date): EP 627487 A2 941207 (Basic)
EP 627487 A3 960821
APPLICATION (CC, No, Date): EP 94303575 940519;

PRIORITY (CC, No, Date): US 68394 930524; US 106463 930812; US 111758 930825; US 162407 931203; US 209502 940307; US 243545 940511
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003078708)
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-013/00; C12P-021/08; A61K-037/02; C12N-015/87;

ABSTRACT EP 627487 A3
Ligands for flt3 receptors capable of transducing self-renewal signals to regulate the growth, proliferation or differentiation of progenitor cells and stem cells are disclosed. The invention is directed to flt3-L as an isolated protein, the DNA encoding the flt3-L, host cells transfected with cDNAs encoding flt3-L, compositions comprising flt3-L, methods of improving gene transfer to a mammal using flt3-L, and methods of improving transplantations using flt3-L. Flt3-L finds use in treating patients with anemia, AIDS and various cancers.
ABSTRACT WORD COUNT: 91

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF2	668
SPEC A	(English)	EPABF2	15742
Total word count - document A			16410
Total word count - document B			0
Total word count - documents A + B			16410

24/3,AB/20 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00629390
G-CSF analog compositions and methods
G-CSF Analoge und Verfahren zu ihrer Herstellung
Analogues de G-CSF et methodes pour les obtenir
PATENT ASSIGNEE:
AMGEN INC., (923238), Amgen Center, One Amgen Center Drive, Thousand Oaks, CA 91320-1789, (US), (Proprietor designated states: all)
INVENTOR:
Osslund, Timothy, 475 Vista Montana, Camarillo, California 93010, (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 612846 A1 940831 (Basic)
EP 612846 B1 000816
APPLICATION (CC, No, Date): EP 94101207 940127;
PRIORITY (CC, No, Date): US 10099 930128
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 890640 (EP 98113221)
EP 965638 (EP 99112115)
EP 974655 (EP 99113571)

INTERNATIONAL PATENT CLASS: C12N-015/27; C12P-021/02; C07K-014/53; G06F-017/50

ABSTRACT EP 612846 A1

Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.

ABSTRACT WORD COUNT: 91

NOTE:

Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200033	367
CLAIMS B	(German)	200033	348
CLAIMS B	(French)	200033	420
SPEC B	(English)	200033	15659
Total word count - document A			0
Total word count - document B			16794
Total word count - documents A + B			16794

24/3,AB/21 (Item 19 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

00502150

DNA CODING FOR GRANULOCYTIC COLONY STIMULATING FACTOR RECEPTOR

FUR DEN REZEPTOR DES GRANULOZYTENKOLONIE STIMULIERENDEN FAKTORS KODIERENDE DNS

CODAGE ADN POUR UN RECEPTEUR DE FACTEUR DE STIMULATION D'UNE COLONIE DE GRANULOCYTES (G-CSF)

PATENT ASSIGNEE:

OSAKA BIOSCIENCE INSTITUTE, (1425270), 2-4, Furaedai 6-chome, Suita-shi, Osaka 565, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

INVENTOR:

NAGATA, Shigekazu, 2-21-17-511, Saidera, Suita-shi, Osaka 565, (JP)

FUKUNAGA, Rikiro, Folk-kitasenri L-302, 5-5, Onohara-higashi, Minoo-shi, Osaka 562, (JP)

LEGAL REPRESENTATIVE:

VOSSIUS & PARTNER (100311), Postfach 86 07 67, 81634 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 521156 A1 930107 (Basic)
EP 521156 A1 930217
EP 521156 B1 990707
WO 9114776 911003

APPLICATION (CC, No, Date): EP 91905894 910322; WO 91JP375 910322

PRIORITY (CC, No, Date): JP 7453990 900323; JP 17662990 900703

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: C07K-014/00; C12P-021/02; C12R-001/19

ABSTRACT EP 521156 A1
A cDNA of a mouse G-CSF receptor is cloned from a library of cDNAs originating in mouse myeloid leukemia cells to analyze its structure. Further, by using this cDNA as the probe, a cDNA of a human G-CSF receptor is cloned from a library of cDNAs originating in human placental or human histocytic lymphoma cells to analyze its structure and at the same time introduce it into a host cell to effect expression. As a result of this expression, it now becomes possible to stably supply a G-CSF receptor useful in both basic research and clinical application. (see image in original document)
ABSTRACT WORD COUNT: 104

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9927	1707
CLAIMS B	(German)	9927	1663
CLAIMS B	(French)	9927	1795
SPEC B	(English)	9927	10513
Total word count - document A			0
Total word count - document B			15678
Total word count - documents A + B			15678

24/3,AB/22 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00485730
Continuous release pharmaceutical compositions comprising a polypeptide covalently conjugated to a water soluble polymer
Pharmazeutische Zusammensetzungen mit kontinuierlicher Abgabe, die mit wasserloslichen Polymeren kovalent gebundene Polypeptide enthalten
Compositions pharmaceutiques a liberation continue comprenant un polypeptide conjuge de maniere covalente a un polymere hydrosoluble
PATENT ASSIGNEE:
AstraZeneca AB, (699188), , 151 85 Sodertalje, (SE), (Proprietor designated states: all)
INVENTOR:
Camble, Roger, 8 Yew Tree Close, Macclesfield, Cheshire SK11 8NY, (GB)
Timms, David, 45 Beech Lane, Macclesfield Cheshire SK10 2DR, (GB)
Wilkinson, Anthony James, 4 Ravenho Lane, Macclesfield, Cheshire, (GB)
LEGAL REPRESENTATIVE:
Mack, John Richard et al (48505), AstraZeneca PLC Global Intellectual Property Mereside Alderley Park, Macclesfield, Cheshire SK10 4TG, (GB)
PATENT (CC, No, Kind, Date): EP 473268 A2 920304 (Basic)
EP 473268 A3 920916
EP 473268 B1 031008
APPLICATION (CC, No, Date): EP 91306452 910716;
PRIORITY (CC, No, Date): GB 9016138 900723; GB 9018414 900823; GB 9018415 900823; GB 9018416 900823; GB 9018417 900823; GB 9018418 900823
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/535; A61K-047/48; A61K-047/32; A61K-038/19

ABSTRACT EP 473268 A2
Pharmaceutical compositions for continuous release of a physiologically active substance in which the physiologically active substance comprises a polypeptide covalently conjugated to a water soluble polymer show particularly desirable release characteristics. Polypeptides for use in the pharmaceutical compositions include G-CSF and solution stable derivatives thereof, human calcitonin and interleukin-2. The material of the composition may be a polylactide or biodegradable hydrogel derived from an amphipathic block copolymer.
The compositions enable a therapeutically effective polypeptide to be continuously released over a prolonged period of time following a single administration of the pharmaceutical composition to a patient. (see image in original document)
ABSTRACT WORD COUNT: 102
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	2057
CLAIMS B	(English)	200341	2105
CLAIMS B	(German)	200341	1956
CLAIMS B	(French)	200341	2375
SPEC A	(English)	EPABF1	42048
SPEC B	(English)	200341	42487
Total word count - document A			44109
Total word count - document B			48923
Total word count - documents A + B			93032

24/3,AB/23 (Item 21 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00483199
Derives du polypeptide G-CSF
G-CSF polypeptide derivatives
G-CSF Polypeptid-Derivate
PATENT ASSIGNEE:
ZENECA LIMITED, (1579441), 15 Stanhope Gate, London W1Y 6LN, (GB),
(applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Camble, Roger, 8 Yew Tree Close, Macclesfield, Cheshire SK11 8NY, (GB)
Wilkinson, Anthony James, 4 Ravenho Lane, Macclesfield, Cheshire, (GB)
Carr, Heather, 16 Princess Street, Bollington, Cheshire, (GB)
Timms, David, 45 Beech Lane, Macclesfield, Cheshire, (GB)
LEGAL REPRESENTATIVE:
Mack, John Richard et al (48504), Intellectual Property Department ZENECA Pharmaceuticals Mereside Alderley Park, Macclesfield, Cheshire SK10 4TG, (GB)
PATENT (CC, No, Kind, Date): EP 459630 A2 911204 (Basic)
EP 459630 A3 921021
EP 459630 B1 980805

APPLICATION (CC, No, Date): EP 91303868 910429;
PRIORITY (CC, No, Date): GB 9009623 900430; GB 9013773 900620; GB 9016215 900724; GB 9102799 910211
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/27; C12P-021/02; C07K-014/535; A61K-038/19;

ABSTRACT EP 459630 A2
Derivatives of naturally occurring G-CSF having at least one of the biological properties of naturally occurring G-CSF, and a solution stability of at least 35% at 5 mg/ml are disclosed in which the derivative has at least Cys(sup 1)(sup 7) of the native sequence replaced by a Ser(sup 1)(sup 7) residue and Asp(sup 2)(sup 7) of the native sequence replaced by a Ser(sup 2)(sup 7) residue.
Nucleotide sequences coding for part or all of the amino acid sequence of the derivatives of the invention may be incorporated into autonomously replicating **plasmid** or viral **vectors** employed to transform or transfect suitable procaryotic or eucaryotic host cells such as bacteria, yeast or vertebrate cells in culture.
ABSTRACT WORD COUNT: 116

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9832	1398
CLAIMS B	(German)	9832	1376
CLAIMS B	(French)	9832	1512
SPEC B	(English)	9832	18965
Total word count - document A			0
Total word count - document B			23251
Total word count - documents A + B			23251

24/3,AB/24 (Item 22 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00452967
GRANULOCYTE-COLONY STIMULATING FACTOR RECEPTORS.
REZEPTOREN FUR GRANULOZYTENKOLONIEN STIMULIERENDEN FAKTOR.
RECEPTEURS DE FACTEURS STIMULANT LES COLONIES DE GRANULOCYTES.
PATENT ASSIGNEE:
IMMUNEX CORPORATION, (485032), Immunex Building 51 University Street, Seattle, WA 98101, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
SMITH, Craig, A., 2405 5th West, Seattle, WA 98119, (US)
LARSEN, Alf, D., 320 Summit Avenue East, 15, Seattle, WA 98104, (US)
SIMS, John, E., 314 Northeast 82nd Street, Seattle, WA 98115, (US)
CURTIS, Benson, M., 1520 Northwest Woodbine Way, Seattle, WA 98177, (US)
LEGAL REPRESENTATIVE:
Froud, Clive et al (51991), Elkington and Fife Prospect House 8 Pembroke Road, Sevenoaks, Kent TN13 1XR, (GB)
PATENT (CC, No, Kind, Date): EP 494260 A1 920715 (Basic)
EP 494260 B1 950614
WO 9105046 910418

APPLICATION (CC, No, Date): EP 90915629 900924; WO 90US5434 900924
PRIORITY (CC, No, Date): US 412816 890926; US 416306 891003; US 522952 900403
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/12; C12P-021/02; C07K-014/705; A61K-038/00; C12P-021/08; G01N-033/68;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	320
CLAIMS B	(German)	EPAB95	279
CLAIMS B	(French)	EPAB95	377
SPEC B	(English)	EPAB95	8778
Total word count - document A			0
Total word count - document B			9754
Total word count - documents A + B			9754

24/3,AB/25 (Item 23 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00394804
Production of pluripotent granulocyte colony-stimulating factor.
Herstellung des die pluripotente Granulozyt-Kolonie stimulierenden Faktors.
Production du facteur de stimulation de colonies de granulocytes pluriactifs.
PATENT ASSIGNEE:
Kirin-Amgen, Inc., (650490), 1900 Oak Terrace Lane, Thousand Oaks California 91320, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Souza, Lawrence M., 417 Camino de Celeste Thousand Oaks, California 91360 , (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Widenmayerstrasse 4/I, D-8000 Munchen 22, (DE)
PATENT (CC, No, Kind, Date): EP 396158 A1 901107 (Basic)
APPLICATION (CC, No, Date): EP 90111660 860822;
PRIORITY (CC, No, Date): US 768959 850823; US 835548 860303
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 237545 (EP 86905530)
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1018552 (EP 2000101091)
(EP 2001118552)
INTERNATIONAL PATENT CLASS: C12N-015/27; C12P-021/02; C07K-013/00; A61K-037/02;

ABSTRACT EP 396158 A1
Disclosed are novel polypeptides possessing part or all of the primary structural conformation and one or more of the biological properties of a mammalian (e.g., human) pluripotent granulocyte colony-stimulating factor ("hpG-CSF") which are characterized in preferred forms by being the

product of procaryotic or eucaryotic host expression of an exogenous DNA sequence. Sequences coding for part or all of the sequence of amino acid residues of hpG-CSF or for analogs thereof may be incorporated into autonomously replicating **plasmid** or viral **vectors** employed to transform or transfect suitable procaryotic or eucaryotic host cells such as bacteria, yeast or vertebrate cells in culture. Products of expression of the DNA sequences display, e.g., the physical and immunological properties and in vitro biological activities of isolates of hpG-CSF derived from natural sources. Disclosed also are chemically synthesized polypeptides sharing the biochemical and immunological properties of hpG-CSF.

ABSTRACT WORD COUNT: 146

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1663
SPEC A	(English)	EPABF1	12124
Total word count - document A			13787
Total word count - document B			0
Total word count - documents A + B			13787

24/3,AB/26 (Item 24 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00365114
Compositions and method for treating or preventing infections in animals.
Zusammensetzungen und Verfahren zur Behandlung oder Verhutung von Infektionen bei Tieren.
Compositions et methode de traitement ou de prevention d'infections chez des animaux.
PATENT ASSIGNEE:
Amgen Inc., (923230), 1900 Oak Terrace Lane, Thousand Oaks, California 91320, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Boone, Thomas C., 3913 Elkwood, Newbury Park California 91320, (US)
Miller, Allan L., 2111 Balmain Way, Glendale California 91206, (US)
Andresen, Jeffrey W., 4601 Student Street, Ventura California 93003, (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Widenmayerstrasse 4/I, D-8000 Munchen 22, (DE)
PATENT (CC, No, Kind, Date): EP 347041 A2 891220 (Basic)
EP 347041 A3 901122
APPLICATION (CC, No, Date): EP 89304853 890512;
PRIORITY (CC, No, Date): US 193857 880513; US 348011 890509
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12P-021/02; C07K-013/00; C12N-015/00; A61K-045/02; A61K-037/02; A61K-045/02; A61K-037/02

ABSTRACT EP 347041 A2
Compositions and method for treating or preventing bacterial infections such as mastitis in animals, particularly bovine animals, which comprises administering an effective amount of granulocyte colony stimulating

factor (G-CSF), are disclosed. The G-CSF may be naturally derived, or alternatively, the G-CSF and genetically engineered variants of G-CSF may be the expression products of genetically engineered prokaryotic or eukaryotic host cells.
ABSTRACT WORD COUNT: 64

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1596
SPEC A	(English)	EPABF1	13007
Total word count - document A			14603
Total word count - document B			0
Total word count - documents A + B			14603

24/3,AB/27 (Item 25 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00351509
Glycosylated polypeptides
Glykosylierte Polypeptide
Polypeptides glycosyles
PATENT ASSIGNEE:
Kyowa Hakko Kogyo Co., Ltd., (229066), 6-1, Ohtemachi 1-chome, Chiyoda-ku, Tokyo 100, (JP), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Sasaki, Katsutoshi, 3-6-6, Asahi-machi, Machida-shi Tokyo, (JP)
Nishi, Tatsunari, 3-9-11, Naka-machi, Machida-shi Tokyo, (JP)
Yasumura, Shigeyoshi, 3-6-6, Asahi-machi, Machida-shi Tokyo, (JP)
Sato, Moriyuki, 2730-15, Naruse, Machida-shi Tokyo, (JP)
Itoh, Seiga, 6-9-48, Aihara, Sagamihara-shi Kanagawa, (JP)
LEGAL REPRESENTATIVE:
Kinzebach, Werner, Dr. et al (6468), Patentanwalte Reitstotter, Kinzebach und Partner Postfach 86 06 49, 81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 370205 A2 900530 (Basic)
EP 370205 A3 900613
EP 370205 B1 980722
APPLICATION (CC, No, Date): EP 89117981 890928;
PRIORITY (CC, No, Date): JP 88245705 880929
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/535; C12N-015/27; C12N-001/21; C12N-005/10; A61K-038/19;

ABSTRACT EP 370205 A2
A polypeptide or glycosylated polypeptide with at least one new carbohydrate chain produced by means of recombinant DNA technique, which has protease resistance and thermal stability and is expected to have longer lifetime in blood than those of a naturally-occurring form.
ABSTRACT WORD COUNT: 45

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count

CLAIMS B	(English)	9830	2052
CLAIMS B	(German)	9830	1823
CLAIMS B	(French)	9830	2191
SPEC B	(English)	9830	27507
Total word count - document A			0
Total word count - document B			33573
Total word count - documents A + B			33573

24/3,AB/28 (Item 26 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00349304
Thrombus control agent.
Mittel zur Kontrolle von Thrombenbildungen.
Agent de controle des formations de thrombus.
PATENT ASSIGNEE:
Chugai Seiyaku Kabushiki Kaisha, (207660), 5-1, 5-chome, Ukima Kita-ku, Tokyo, (JP), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
INVENTOR:
Tsuji, Koichiro, 6598, Toyota, Suwa-shi Nagano-ken, (JP)
Ono, Masayoshi, 1369-7, Yamaguchi, Tokorozawa-shi Saitama-ken, (JP)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, D-81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 355811 A2 900228 (Basic)
EP 355811 A3 910320
EP 355811 B1 931201
APPLICATION (CC, No, Date): EP 89115562 890823;
PRIORITY (CC, No, Date): JP 88210376 880824
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-037/02; A61K-047/00; C12P-021/08;
ABSTRACT EP 355811 A2

A thrombus control agent is disclosed which comprises a human granulocyte colony stimulating factor (human G-CSF) as an active ingredient and a pharmaceutically acceptable carrier. This thrombus control agent can be administered to a patient bearing thrombi formed in the arterial and venous vessels. Furthermore, the use of human G-CSF for preparing the thrombus control agent is disclosed.

The inventors found that human G-CSF is useful for treating thrombi and developed the use of human G-CSF for this purpose although nobody has clearly reported this type of pharmacological activity of human G-CSF.

ABSTRACT WORD COUNT: 96

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	348
CLAIMS B	(German)	EPBBF1	328
CLAIMS B	(French)	EPBBF1	430
SPEC B	(English)	EPBBF1	3971
Total word count - document A			0
Total word count - document B			5077
Total word count - documents A + B			5077

24/3,AB/29 (Item 27 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00310979
Leukaemia inhibitory factor.
Leukamie hemmender Faktor.
Facteur d'inhibition de la leucemie.
PATENT ASSIGNEE:
AMRAD CORPORATION LIMITED, (960661), 17-27 Cotham Road, Kew, VIC 3101, (AU), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Gearing, David Paul, 134 Miller Street North Fitzroy, Victoria, (AU)
Gough, Nicholas Martin, 20 Rangeview Grove North Balwyn, Victoria, (AU)
Hilton, Douglas James, 8 West End Road Warrandyte, Victoria, (AU)
King, Julie Ann, 121 Springvale Road Nunawading, Victoria, (AU)
Metcalf, Donald, 268 Union Road Balwyn, Victoria, (AU)
Nice, Edouard Collins, 9 Odessa Street St. Kilda, Victoria, (AU)
Nicola, Nicos Anthony, 59 Queen Street Regent, Victoria, (AU)
Simpson, Richard John, 42 Stanley Street Richmond, Victoria, (AU)
Willson, Tracy Ann, 26 Fortuna Avenue North Balwyn, Victoria, (AU)
LEGAL REPRESENTATIVE:
Holmes, Michael John et al (31971), Frank B. Dehn & Co. Imperial House 15-19 Kingsway, London WC2B 6UZ, (GB)
PATENT (CC, No, Kind, Date): EP 285448 A2 881005 (Basic)
EP 285448 A3 900829
EP 285448 B1 940316
APPLICATION (CC, No, Date): EP 88302962 880331;
PRIORITY (CC, No, Date): AU 871209 870402; AU 873317 870724; AU 874903 871015; AU 876005 871221
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; C12P-021/00; A61K-037/02; C12Q-001/68;

ABSTRACT EP 285448 A2
A leukaemia-inhibitory factor (LIF) is disclosed, together with a method of preparation of LIF in essentially pure form. Nucleotide and amino acid sequences are disclosed, together with recombinant DNA molecules and host cells for production of polypeptides having LIF activity.
ABSTRACT WORD COUNT: 44

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	4613
CLAIMS B	(German)	EPBBF1	4278
CLAIMS B	(French)	EPBBF1	5293
SPEC B	(English)	EPBBF1	17225
Total word count - document A			0
Total word count - document B			31409
Total word count - documents A + B			31409

Searcher : Shears 571-272-2528

24/3,AB/30 (Item 28 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00265374
Novel polypeptide
Neues Polypeptid
Nouveau polypeptide
PATENT ASSIGNEE:
KYOWA HAKKO KOGYO CO., LTD., (229062), 6-1, Ohtemachi 1-chome, Chiyoda-ku, Tokyo-to, (JP), (applicant designated states: BE;CH;DE;ES;FR;GB;IT;LI;NL;SE)
INVENTOR:
Kuga, Tetsuro, 2-3-107, Kyowa-cho, Hofu-shi Yamaguchi, (JP)
Komatsu, Yoshinori, 1845-1, Honmachida, Machida-shi Tokyo, (JP)
Miyaji, Horomasa, 4-9-14 Naka-machi, Machida-shi Tokyo, (JP)
Sato, Moriyuki, 2-13-1, Naruse, Machida-shi Tokyo, (JP)
Okabe, Masami, 410-1, Nameri Nagaizumi-cho, Suntogun Shizuoka, (JP)
Morimoto, Makoto, 203-5, Shimotogari Nagaizumi-cho, Sunto-gun Shizuoka, (JP)
Itoh, Seiga, 218-14, Aza Hachiman Nishi Aihara, Sagamihara-shi Kanagawa, (JP)
Yamasaki, Motoo, 3-6-6, Asahi-machi, Machida-shi Tokyo, (JP)
Yokoo, Yoshiharu, 3-4-17, Yokoyama, Sagamihara-shi Kanagawa, (JP)
Yamaguchi, Kazuo, 2121-8, Isobe, Sagamihara-shi Kanagawa, (JP)
LEGAL REPRESENTATIVE:
Kinzebach, Werner, Dr. et al (6468), Patentanwalte Reitstotter, Kinzebach und Partner Postfach 86 06 49, 81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 272703 A1 880629 (Basic)
EP 272703 B1 930728
APPLICATION (CC, No, Date): EP 87119157 871223;
PRIORITY (CC, No, Date): JP 86306799 861223
DESIGNATED STATES: BE; CH; DE; ES; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/70

ABSTRACT EP 272703 A1
Novel hG-CSF polypeptide derivatives having an amino acid sequence derived from the amino acid sequence of the human granulocyte colony stimulating factor polypeptide by substitution of at least one amino acid by a different aminoacid and/or deletion of at least one amino acid, recombinant plasmids containing a DNA fragment insert coding for any of these hG-CSF polypeptide derivatives, microorganisms carrying one of such plasmids, and methods of producing the hG-CSF polypeptide derivatives using the microorganisms are described.
ABSTRACT WORD COUNT: 81

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9710W2	1866
CLAIMS B	(German)	9710W2	1625
CLAIMS B	(French)	9710W2	2061
SPEC B	(English)	9710W2	23511
Total word count - document A			0
Total word count - document B			29063
Total word count - documents A + B			29063

Searcher : Shears 571-272-2528

24/3,AB/31 (Item 29 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00235122
PRODUCTION OF PLURIPOTENT GRANULOCYTE COLONY-STIMULATING FACTOR
HERSTELLUNG VON PLURIPOTENTEN GRANULOZYTKOLONIE ERREGENDEM FAKTOR
PRODUCTION DU FACTEUR DE STIMULATION DE COLONIES DE GRANULOCYTES PLURIPOTENTS
PATENT ASSIGNEE:
Kirin-Amgen, Inc., (650490), 1900 Oak Terrace Lane, Thousand Oaks California 91320, (US), (Proprietor designated states: all)
INVENTOR:
SOUZA, Lawrence, M., 1302 Witherspoon, Thousand Oaks, CA 91360, (US)
LEGAL REPRESENTATIVE:
Brown, John David et al (28811), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 237545 A1 870923 (Basic)
EP 237545 A1 880203
EP 237545 B1 910522
EP 237545 B2 990825
WO 8701132 870226
APPLICATION (CC, No, Date): EP 86905530 860822; WO 86US1708 860822
PRIORITY (CC, No, Date): US 768959 850823; US 835548 860303
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 396158 (EP 90111660)
INTERNATIONAL PATENT CLASS: C12N-015/27; C12P-019/34; C12P-021/02; C07K-014/535; A61K-038/17
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9934	1911
CLAIMS B	(German)	9934	1891
CLAIMS B	(French)	9934	2148
SPEC B	(English)	9934	11918
Total word count - document A			0
Total word count - document B			17868
Total word count - documents A + B			17868

24/3,AB/32 (Item 30 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00231813
HUMAN GRANULOCYTE COLONY STIMULATING FACTOR.
MENSCHLICHER GRANULOXCYT-KOLONIE-STIMULIERUNGSFAKTOR.
FACTEUR DE STIMULATION DE COLONIES DE GRANULOCYTES HUMAINS.
PATENT ASSIGNEE:
Chugai Seiyaku Kabushiki Kaisha, (207660), 5-1, 5-chome, Ukima Kita-ku, Tokyo, (JP), (applicant designated states:

AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
INVENTOR:
ONO, Masayoshi Chugai Seiyaku Kabushiki Kaisha, 41-8, Takada 3-chome, Toshima-ku Tokyo 171, (JP)
NOMURA, Hitoshi Chugai Seiyaku Kabushiki Kaisha, 41-8, Takada 3-chome Toshima-ku, Tokyo 171, (JP)
TAMURA, Masahiko Chugai Seiyaku Kabushiki Kaisha, 41-8, Takada 3-chome, Toshima-ku Tokyo 171, (JP)
MATSUMOTO, Masahiko, Chugai Seiyaku Kabushiki Kaisha 41-8Takada 3chome, Toshima-ku Tokyo 171, (JP)
YAMAZAKI, Tatsumi, Chugai Seiyaku Kabushiki Kaisha 41-8Takada 3chome, Toshima-ku Tokyo 171, (JP)
YAMAMOTO, Osami, Chugai Seiyaku Kabushiki Kaisha 41-8Takada 3chome, Toshima-ku Tokyo 171, (JP)
HIRATA, Yuichi, Chugai Seiyaku Kabushiki Kaisha 41-8Takada 3chome, Toshima-ku Tokyo 171, (JP)
SEKIMORI, Yasuo, Chugai Seiyaku Kabushiki Kaisha 41-8Takada 3chome, Toshima-ku Tokyo 171, (JP)
TSUCHIYA,Masayuki Chugai Seiyaku Kabushiki Kaisha, 41-8, Takada 3-chome Toshima-ku, Tokyo 171, (JP)
NAGATA, Shigekazu, 24-62-3-305, Tamagawa 2-chome, Ohta-ku Tokyo 146, (JP)
LEGAL REPRESENTATIVE:
Vossius & Partner (100311), Siebertstrasse 4 P.O. Box 86 07 67, W-8000 Munchen 86, (DE)
PATENT (CC, No, Kind, Date): EP 215126 A1 870325 (Basic)
EP 215126 A1 871125
EP 215126 B1 910731
WO 8604605 860814
APPLICATION (CC, No, Date): EP 86901138 860207; WO 86JP52 860207
PRIORITY (CC, No, Date): JP 8523777 850208; JP 85206066 850917; JP 85209638 850920; JP 85269455 851202; JP 85269456 851202; JP 85270838 851203; JP 85270839 851203
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/27; C07K-013/00; A61K-037/02;

ABSTRACT EP 215126 A1
HUMAN GRANULOCYTE COLONY STIMULATING FACTOR.
A gene which codes a polypeptide having a **human granulocyte colony stimulating** activity, a **recombinant** vector having said gene incorporated therein, a transformant containing said vector, a polypeptide or glycoprotein yielded from said transformant and having human granulocyte colony stimulating activity, and in infection inhibitor containing human granulocyte colony stimulating factor as an effective ingredient. Said stimulating factor includes one obtained by the gene recombination technology and one obtained from the supernatant of a culture medium of cells yielding a human granular colony stimulating factor.
ABSTRACT WORD COUNT: 92

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	293
CLAIMS B	(German)	EPBBF1	271
CLAIMS B	(French)	EPBBF1	357
SPEC B	(English)	EPBBF1	21118

Searcher : Shears 571-272-2528

Total word count - document A 0
Total word count - document B 22039
Total word count - documents A + B 22039

24/3,AB/33 (Item 31 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00208929
Pharmaceutical composition containing a human granulocyte colony stimulating factor for the treatment of leukopenia
Einen menschlichen Granulozytkoloniereizfaktor fur die Behandlung von Leukopenien enthaltende pharmazeutische Zubereitung
Composition pharmaceutique contenant un facteur stimulant les colonies de granulocyte pour le traitement de leucopenies
PATENT ASSIGNEE:
Chugai Seiyaku Kabushiki Kaisha, (207660), 5-1, 5-chome, Ukima Kita-ku, Tokyo, (JP), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;NL;SE)
INVENTOR:
Tamura, Masahiko, Sahoda roiyaruhaitsu 302 Kuji 14 Takatsu-ku, Kawasaki-shi Kanagawa-ken, (JP)
Nomura, Hitoshi, 3-11-16-218, Igusa Suginami-ku, Tokyo, (JP)
Hattori, Kunihiro, Chugai inokashiraryo 2-20-9, Inokashira, Mitaka-shi Tokyo, (JP)
Ono, Masayoshi, 1369-7, Yamaguchi, Tokorozawa-shi Saitama-ken, (JP)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, 81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 217404 A2 870408 (Basic)
EP 217404 A3 880713
EP 217404 B1 920115
APPLICATION (CC, No, Date): EP 86113671 861003;
PRIORITY (CC, No, Date): JP 85220450 851004; JP 86125660 860602
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C12P-021/02

ABSTRACT EP 217404 A2
Described is a novel leukopenia treating agent containing a human granulocyte colony stimulating factor (human G-CSF) as an effective ingredient.
Human G-CSFs which are suitable for use in a leukopenia treating agent of the present invention include ones obtained by isolation from the supernatant of a culture of a human G-CSF producing cell, and a polypeptide or glycoprotein having G-CSF activity that is obtained by transforming a host with a recombinant vector having incorporated therein a gene coding for a polypeptide having the human G-CSF activity.
ABSTRACT WORD COUNT: 90

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9901	778
CLAIMS B	(German)	9901	725
CLAIMS B	(French)	9901	941
SPEC B	(English)	9901	9454

Searcher : Shears 571-272-2528

Total word count - document A 0
Total word count - document B 11898
Total word count - documents A + B 11898

24/3,AB/34 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0326294 DBR Accession No.: 2003-27435 PATENT
Method for producing human granulocyte-macrophage colony stimulating factor and recombinant human granulocyte-macrophage colony stimulating factor protein by using the plant cell suspension culture - recombinant protein production via plasmid expression in plant suspension cell culture
AUTHOR: JANG Y S; KWON T H; YANG M S
PATENT ASSIGNEE: JANG Y S; KWON T H; YANG M S 2002
PATENT NUMBER: KR 2002094818 PATENT DATE: 20021218 WPI ACCESSION NO.: 2003-774890 (200373)
PRIORITY APPLIC. NO.: KR 33273 APPLIC. DATE: 20010613
NATIONAL APPLIC. NO.: KR 33273 APPLIC. DATE: 20010613
LANGUAGE: KR
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Provided are a method for producing human granulocyte-macrophage colony stimulating factor and a recombinant human granulocyte-macrophage colony stimulating factor protein by using the plant cell suspension culture, thereby cheaply mass producing the **human granulocyte colony stimulating** factor. DETAILED DESCRIPTION - A **recombinant** vector pMY064 contains a gene encoding human granulocyte-macrophage colony stimulating factor(hGM-CSF) having the nucleotide sequence of SEQ ID NO: 1. A transformed plant cell is produced by transforming a plant cell with the recombinant vector pMY064, wherein the transformed plant cell is Nicotiana tabacum pMYO64(KCTC 0670BP). The recombinant human granulocyte-macrophage colony stimulating factor protein is produced by the suspension culture of the plant cell Nicotiana tabacum pMYO64(KCTC 0670BP), wherein the suspension culture is carried out by further addition of 0.1 to 5 g/l of polyvinyl pyrrolidine into an MS medium.(1 pages)

24/3,AB/35 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0293624 DBR Accession Number: 2002-15471 PATENT
DNA cassette, useful as promoter in producing mammalian **recombinant** protein, such as **human granulocyte colony stimulating** factor, comprises lac promoter, spacer region and neutral protease promoter in 5' to 3' direction - recombinant protein production via plasmid expression in bacterium cell
AUTHOR: NAITOU N; MATSUMOTO K; HIGASHIMURA N; TSUNEKAWA B; UCHIDA H; WADA M
PATENT ASSIGNEE: MITSUI CHEM INC 2002
PATENT NUMBER: EP 1195437 PATENT DATE: 20020410 WPI ACCESSION NO.: 2002-354155 (200239)
PRIORITY APPLIC. NO.: JP 2000305132 APPLIC. DATE: 20001004

NATIONAL APPLIC. NO.: EP 2001308502 APPLIC. DATE: 20011004
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A DNA cassette (I) functioning as a promoter for protein expression in Escherichia coli, comprising a promoter derived from a lac promoter region in a pUC 19 plasmid, a spacer region and a second promoter derived from a promoter region in a neutral protease in Bacillus amyloliquefaciens, where the first promoter, spacer and second promoter are sequentially aligned in series in a 5' to 3' direction, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a plasmid comprising (I) and a region permitting replication in E. coli; (2) an E. coli comprising (1); (3) a recombinant plasmid for protein expression in E. coli comprising (I), a coding region encoding a protein which is functionally ligated to the 3' end in (I) and a region for replication in E. coli; (4) a recombinant E. coli which is transformed with (3) and can produce the protein encoded in the coding region; and (5) producing a protein comprising culturing (4) to produce the protein encoded in the coding region in the recombinant plasmid, carried by the recombinant E. coli within the cells of the E. coli, and recovering the protein from the cells. BIOTECHNOLOGY - Preferred Cassette: The first promoter has a fully defined sequence of 213 base pairs (bp) as given in the specification. The spacer region is a DNA of 25 - 45 bp, preferably from the 5' end of a lacZ gene in the pUC19 plasmid. The second promoter has a fully defined sequence of 84 or 144 bp as given in the specification. (I) has a fully defined sequence of 337 bp as given in the specification. Preferred Plasmid: In (3), the protein is derived from a mammal. The protein is human granulocyte colony stimulating factor (hG-CSF), human fibroblast growth factor (hFGF-2), or canine growth hormone. Preparation: No preparative details for (I) are given. USE - (I) is used as a promoter to produce a mammalian protein, such as human granulocyte colony stimulating factor (hG-CSF), human fibroblast growth factor (hFGF-2), or canine growth hormone, in Escherichia coli, and the protein can then be recovered (claimed). ADVANTAGE - (I) can be used to achieve a higher productivity of a protein derived from a mammal in Escherichia coli. The need for adding an inducer, such as isopropylthio-galactopyranoside (IPTG) for producing the protein, is eliminated and a desired protein may be gradually accumulated within cells as culturing proceeds. EXAMPLE - None given in the source material. (34 pages)

24/3,AB/36 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0292900 DBR Accession Number: 2002-14747 PATENT
New human granulocyte colony stimulating factor analogs comprising a substitution of aspartic acid with histidine at amino acid residues 109, 112 or 119, useful for in replacement therapy protocols for treating e.g. neutropenia - virus **vector** or **plasmid** -mediated gene transfer and expression in Escherichia coli, mammal, cancer, yeast or insect cell or hematopoietic stem cell for use in therapy and gene therapy
AUTHOR: SARKAR C A; LAUFFENBURGER D A; TIDOR B
PATENT ASSIGNEE: AMGEN INC 2002
PATENT NUMBER: WO 200220766 PATENT DATE: 20020314 WPI ACCESSION NO.:

2002-415729 (200244)
PRIORITY APPLIC. NO.: US 231464 APPLIC. DATE: 20000908
NATIONAL APPLIC. NO.: WO 2001US28602 APPLIC. DATE: 20010910
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A human granulocyte colony stimulating factor (G-CSF) analog polypeptide (I) comprising an amino acid substitution, is new. DETAILED DESCRIPTION - A human granulocyte colony stimulating factor (G-CSF) analog polypeptide (I) comprises an amino acid substitution in the fully defined 174 amino acid sequence given in the specification, selected from a substitution of aspartic acid with histidine at position 109, (His 109)G-CSF; at position 112, (His112)G-CSF; at position 119 (His119)G-CSF; or any of their subparts optionally including an N-terminal methionyl residue. INDEPENDENT CLAIMS are also included for the following: (1) a G-CSF analog polypeptide of claim I derivatized with one or more water-soluble polymers; (2) a polynucleotide encoding (I); (3) an expression construct containing a polynucleotide of (2); (4) a host cell containing a polynucleotide of (2); (5) a process for producing G-CSF analog polypeptides (His109)G-CSF, (His112)G-CSF, (His119)G-CSF, or the Met-1 species, from a host cell containing nucleic acid encoding such analogs, by culturing the host cell containing (I) to facilitate the expression of the polypeptide, and obtaining the G-CSF analog polypeptide; (6) a method (M1) of treating a hematopoietic, neurological or reproduction related condition by administering a composition comprising (I) to the patient; (7) a method (M2) of sensitizing cells to chemotherapy and radiotherapy by administering a composition comprising (I) to a patient; (8) a method (M3) for culturing hematopoietic cells in vitro by placing the cells in a culture medium containing a G-CSF analog polypeptide, and growing hematopoietic cells; and (9) a kit containing components for culturing hematopoietic cells comprising: (a) an analog polypeptide (I); (b) components for preparing medium for culturing hematopoietic cells; and (c) optionally, at least one additional factor selected from erythropoietin (EPO), G-CSF, stem cell factor (SCF), megakaryocyte-growth and differentiation factor (M-GDF), GM-CSF, M-CSF, CSF-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, 11,-9, IL-10, IL-11, IL-12, Interleukins, IGF-1, leukemia inhibitory factor (LIF), interferon, a neurotrophic factor, flt-3/flk-2 ligand, and a fibroblast growth factor. BIOTECHNOLOGY - Preparation: G-CSF analogs were prepared by either insertional or site-directed mutagenesis of DNA encoding r-met-HuG-CSF using the polymerase chain reaction overlap extension method. Preferred Analog Polypeptide: The G-CSF analog polypeptide is derivatized with one or more water-soluble polymers. Preferred Polynucleotide: The polynucleotide molecule is selected from a DNA comprising: (a) a sequence selected from three fully defined 565 nucleotide sequences given in the specification, or their complements; and (b) any of the DNA sequences of subpart (a) additionally encoding an N- terminal methionyl residue. Preferred Host Cell: The host cell is a bacterium, mammalian, cancer, yeast, or insect cell. Preferred Method: In M1 and M2, treatment, and sensitizing or culturing of cells further includes the use of at least one additional factor selected from EPO, G-CSF, SCF, M-GDF, GM-CSF, M-CSF, CSF-1, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, Interleukins, IGF-1, LIF, interferon, a neurotrophic factor, flt-3/flk-2 ligand, and a fibroblast growth factor. ACTIVITY - Immunostimulant; hemostatic; antianemic; antibacterial; immunosuppressive; anti-HIV; osteopathic.

MECHANISM OF ACTION - G-CSF agonist. USE - The G-CSF analogs are useful for treating hematopoietic, neurological or reproduction related conditions, including reduced hematopoietic function, immune function, neutrophil count or neutrophil mobilization, mobilization of peripheral blood progenitor cells, sepsis, severe chronic neutropenia, bone marrow transplants, infectious diseases, leucopenia, thrombocytopenia, anemia, enhanced engraftment of bone marrow during transplantation, enhanced bone marrow recovery in treatment of radiation, chemical or chemotherapeutic induced bone marrow aplasia or myelosuppression, and acquired immune deficiency syndrome. G-CSF analogs may be also used in replacement therapy protocols for the treatment of neutropenia, and in gene therapy setting. DNA sequences are useful in generating new and useful viral and **plasmid** DNA **vectors** and host cells. ADMINISTRATION - Administration is by intravenous, intradermal, intramuscular, intramammary, intraperitoneal, intrathecal, retrobulbar, intrapulmonary, oral, sublingual, nasal, anal, vaginal or transdermal delivery, or by surgical implantation at a particular site. Dosage is 0.001-1000 microg/kg body weight per day. ADVANTAGE - The G-CSF analog polypeptides demonstrate advantages in stability, which are not seen in other G-CSF species, and provide enhanced cellular response (superagonist or G-CSF agonist type activity) as compared to wild type G-CSF. EXAMPLE - Granulocyte colony stimulating factor (G-CSF) analogs were prepared by either insertional or site-directed mutagenesis of DNA encoding r-met-HuG-CSF using the polymerase chain reaction overlap extension method. After confirming mutations by sequence analysis, each of the mutants was expressed in Escherichia coli K12, refolded, and purified. The DNA encoding **recombinant human G-CSF** had an initial methionine codon followed by codons for the 174-amino acid species of human G-CSF. The purified r-met-HuG-CSF analogs retain the initiating Met (position Met-1). Each of the G-CSF analogs with a substitution of aspartic acid with histidine at position 109, (His 109)G-CSF, at position 112, (His112)G-CSF, and at position 119 (His119)G-CSF, comprises a fully defined sequence of 565 nucleotides encoding a protein having a sequence of 174 amino acids given in the specification. Confirmation of the identity of the G-CSF analogs was accomplished by N-terminal amino acid sequencing of intact proteins. Sequences of the purified G-CSF analogs matched the sequences predicted from the respective DNA sequences. (69 pages)

24/3,AB/37 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0241854 DBR Accession Number: 1999-11955
Purification and characterization of **recombinant human granulocyte colony stimulating** factor (rhG-CSF) derivatives: KW-2228 and other derivatives - protein production via **vector plasmid** pCfBD28-mediated gene transfer and expression in Escherichia coli
AUTHOR: Yamasaki M; Konishi N; Yamaguchi K; Itoh S; Yokoo Y
CORPORATE AFFILIATE: Kyowa-Hakko
CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., 3-6-6 Asahi-machi, Machida-shi, Tokyo 194-8533, Japan.
JOURNAL: Biosci.Biotechnol.Biochem. (62, 8, 1528-34) 1998
ISSN: 0916-8451 CODEN: BBBIEJ

LANGUAGE: English
ABSTRACT: Various derivatives of **recombinant human granulocyte colony stimulating** factor (rhG-CSF) were overproduced in Escherichia coli K12-MM-294 cells with the strong, inducible trp promoter. **Vector plasmid** pCfBD28, which contained which contained the gene for KW-2228 rhG-CSF derivative, under the control of the trp promoter, was constructed and used to transform the E. coli cells. The transformed cells were cultured in M9 culture medium at 33 deg overnight. When the OD of the culture reached over 10 at 550 nm, 20 ug/ml indoleacrylic acid was added to the culture in order to induce protein overexpression. The M9 culture medium contained (%) 0.5 casamino acids, 0.5 glucose, 4 ug/ml thiamine and 50 ug/ml ampicillin. 1 Hour after induction the cells were harvested and KW-2228 was purified from the culture medium using a process involving a sequential renaturation process and 3-step chromatography. KW-2228 was purified to over 99%, determined using SDS-PAGE and HPLC analysis. Circular dichroism and NMR spectroscopy analysis suggested that rhG-CSF and KW-2228 had very similar conformations, but there were 5 amino acid substitutions between the 2. (26 ref)

24/3,AB/38 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0232489 DBR Accession Number: 99-02590 PATENT
New expression vectors comprising yeast-derived promoter and secretion signals - human recombinant somatotropin and granulocyte colony stimulating factor production via **vector plasmid**-mediated gene transfer expression in Saccharomyces cerevisiae
AUTHOR: Jang K R; Moon J W; Bae C S; Yang D S; Lee J W; Seong B L
CORPORATE SOURCE: Masan-si, Korea.
PATENT ASSIGNEE: Hanil-Synth.Fiber 1998
PATENT NUMBER: WO 9854339 PATENT DATE: 981203 WPI ACCESSION NO.: 99-059845 (9905)
PRIORITY APPLIC. NO.: KR 97 APPLIC. DATE: 970527
NATIONAL APPLIC. NO.: WO 97KR97 APPLIC. DATE: 970527
LANGUAGE: English
ABSTRACT: An expression vector containing a yeast-derived promoter and secretion signal, is new. Also claimed are Saccharomyces cerevisiae transformants with the following KCTC accession numbers; 0195 BP, 0193 BP, 0194 BP, 0330 BP and 0331 BP, which were transformed with plasmid YEp2kIL20GC, plasmid pIL20GC, plasmid YEpHSPGC, plasmid pIL20XGC and **plasmid** pIL20XGH, respectively. The **vectors** may be used to produce **recombinant** proteins, particularly human somatotropin and **human granulocyte colony stimulating** factor from yeast. These vectors have the advantage of being arranged in such a way as to facilitate high levels of expression and secretion of heterologous proteins, once transformed into yeast cells. In the preferred vector the promoter is a hybrid consisting of GAL1-10 UAS and mating factor-1 promoter. The secretion signal consists of the killer toxin secretion signal and 24 amino acids of the amino terminal of interleukin-1 (optimized by yeast codon usage). The vector also contains a transcription terminator (from GAPDH) and a GAL4 gene. The vectors were prepared using conventional recombinant techniques. (91pp)

24/3,AB/39 (Item 6 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0183828 DBR Accession Number: 95-10649
High level expression and simple purification of **recombinant human granulocyte colony stimulating** factor in E. coli - human recombinant protein over-production by **vector plasmid** pCSF451 expression in Escherichia coli, and purification
AUTHOR: Kang S H; Na K H; Park J H; Park C I; Lee S Y; Lee Y I
CORPORATE AFFILIATE: Dong-A-Pharm. Univ.Korea Korea-Res.Inst.Biosci.Biotechnol.
CORPORATE SOURCE: Research Laboratories of Dong-A Pharm. Co., Ltd., Yongin-Kun, Kyunggi-Do, 449-900, Korea.
JOURNAL: Biotechnol.Lett. (17, 7, 687-92) 1995
ISSN: 0141-5492 CODEN: BILED3
LANGUAGE: English
ABSTRACT: A 540 bp fragment encoding the human granulocyte colony stimulating factor (CSF) gene was isolated from plasmid pCSF18. The DNA fragment was then subcloned between ClaI and SalI sites of plasmid pDA103 to form plasmid pCSF451 which was expressed in Escherichia coli W3110. The transformed bacterium was then fed-batch cultured in medium containing 30 g/l bacto tryptone, 5 g/l yeast extract, 10 g/l glucose and trace metal solution. A 25% casamino acid solution (which lacked tryptophan) was used as the N-source of the feed medium to induce CSF production. 3-Beta-indoleacrylic acid was added to 1 mM at the early log phase of growth, and incubated for an additional 6 hr. Cells were then centrifuged and the solution of inclusion bodies was diluted with 4 volumes of deionized water (pH 10.0) within 30 min after solubilization and renatured spontaneously for 16 hr at RT. The renaturation process was terminated by pH shift to 5.5. CSF was purified to 99% by SP-Sepharose and ammonium sulfate chromatography to yield 500-600 mg/l culture. (10 ref)

24/3,AB/40 (Item 7 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0165465 DBR Accession Number: 94-08016
Regulation of **recombinant human granulocyte colony stimulation** factor production using herpes simplex virus-1 thymidine-kinase gene - granulocyte colony stimulating factor regulation in NIH3T3 cell culture; regulatory method potentially applicable to cytokine supplement gene therapy
AUTHOR: Aoki Y; Tani K; Takahashi K; Fukushima M; Ozawa K; +Asano S
CORPORATE AFFILIATE: Univ.Tokyo-Inst.Med.Sci. Chugai-Pharm.
CORPORATE SOURCE: Department of Hematology-Oncology, The Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108, Japan.
JOURNAL: Biochem.Biophys.Res.Commun. (200, 3, 1245-51) 1994
CODEN: BBRCA9
LANGUAGE: English
ABSTRACT: The feasibility of applying a suicide vector system for the regulation of foreign gene expression at a cellular level was

determined. The system depended on the introduction of a herpes simplex virus (HSV)-thymidine-kinase (TK, EC-2.7.1.21)-coding **plasmid vector** followed by ganciclovir (GCV) treatment. Thus, HSV-TK expression plasmid M2 or plasmid pRSV-TK was cotransfected with plasmid pY3 into human recombinant granulocyte colony stimulating actor (rhG-CSF)-producing NIH3T3 fibroblast cell line No.14. M2 used the TK promoter to express the HSV-TK gene. In pRSV-TK, the HSV-TK fragment from M2 was inserted into plasmid pRSVcat under the control of the Rous-sarcoma virus long terminal repeat. Clones No.14-M2 and No.14-RT were selected. These cell lines showed an over 100-fold increase in sensitivity (ID50 below 1.6 uM) to GCV compared with the parent cell line. rhG-CSF production by No.14-RT and No.14-M2 cells was strongly suppressed by GCV treatment; rhG-CSF levels in culture supernatants were suppressed by over 50% at 1.6 uM GCV and over 80% at 8 uM GCV. This regulatory method may be applicable to cytokine supplement gene therapy. (20 ref)

24/3,AB/41 (Item 8 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0114637 DBR Accession Number: 91-02279 PATENT
Production of a recombinant protein by transformed animal cell culture - tumor necrosis factor, lymphotoxin, etc. induction of enzyme, enzyme-inhibitor, cytokine or immunoglobulin, e.g. colony stimulating factor and prourokinase, in Namalwa or CHO cell culture
PATENT ASSIGNEE: Kyowa-Hakko 1990
PATENT NUMBER: JP 2257891 PATENT DATE: 901018 WPI ACCESSION NO.: 90-357863 (9048)
PRIORITY APPLIC. NO.: JP 8978573 APPLIC. DATE: 890331
NATIONAL APPLIC. NO.: JP 8978573 APPLIC. DATE: 890331
LANGUAGE: Japanese
ABSTRACT: Animal cell cultures are stimulated to produce recombinant protein, e.g. enzyme, enzyme-inhibitor, cytokine or immunoglobulin, by the addition of 10-10 million U/ml, preferably 100-10,000 U/ml cytokine, preferably human tumor necrosis factor, lymphotoxin, or a lymphotoxin derivative (with 11 or 22 amino acids deleted from the N-terminus of the mature lymphotoxin) to the culture medium. The animal cell culture is preferably Chinese hamster ovary (CHO) or human Namalwa cell culture. The cytokines induce the formation of useful recombinant proteins in the new, efficient culture method. The method may be used to prepare human granulocyte colony stimulating factor or human pro-urokinase (EC-3.4.21.31), which may be recovered in crude form or isolated and purified. The promoter of the plasmid used to transform the animal cells is preferably the SV40 virus early or late promoter, Moloney mouse leukemia virus long terminal repeat, part of the human T-lymphocyte leukemia virus-I long terminal repeat containing the SV40 virus early promoter, especially the latter. The animal cell may be proliferated prior to culture in cytokine-containing medium. (48pp)

24/3,AB/42 (Item 9 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0103509 DBR Accession Number: 90-06200
Effect of N-terminal deletion of signal peptide on the secretion of human granulocyte colony stimulating factor in mammalian cells - human recombinant granulocyte colony stimulating factor protein secretion by CHO cell culture transformed with **vector plasmid** pSe1GC3-3dhfr and **plasmid** pSE1GC4-2dhfr
AUTHOR: Kuga T; Komatsu Y; Mizukami T; Sato M; +Itoh S
CORPORATE AFFILIATE: Kyowa-Hakko
CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., 3-6-6 Asahimachi, Machidashi, Tokyo 194, Japan.
JOURNAL: Biotechnol.Lett. (12, 2, 87-92) 1990
CODEN: BILED3
LANGUAGE: English
ABSTRACT: The effect of deletion of the non-conserved N-terminus of the signal peptide of **human granulocyte colony stimulating** factor (G-CSF) on secretion of the **recombinant** protein from mammalian cells was investigated. 6 Synthetic oligonucleotides were inserted between SalI and ApaLI sites of the cDNA clone, plasmid pCSF2, which lacked a coding region for the N-terminal 20 amino acids of the signal peptide. The resultant plasmid pCSF3-3 was used to construct the N-terminal deletion mutant plasmid pCSF4-2. SalI-BamHI fragments of these **plasmids** were inserted into expression **vectors** to give **plasmid** pSe1GC3-3dhfr and plasmid pSE1GC4-2dhfr, respectively. Dihydrofolate-reductase (EC-1.5.1.3)-deficient CHO cells were transfected with each plasmid, and the supernatants of transformants were assayed for G-CSF activity. The 9 N-terminal amino acids of the signal peptide were not required for human recombinant G-CSF secretion although the productivity was rather low. This low productivity was not due to the low efficiency of secretion because the plasmid copy number of each cDNA in transformants was not determined. (13 ref)

24/3,AB/43 (Item 10 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0083928 DBR Accession Number: 89-01919
Alteration of amino-terminal codons of human granulocyte colony stimulating factor increases expression levels and allows efficient processing by methionine-aminopeptidase in Escherichia coli - gene cloning and site-directed mutagenesis
AUTHOR: Devlin P E; Drummond R J; Toy P; Mark D F; Watt K W K; Devlin J J
CORPORATE AFFILIATE: Cetus
CORPORATE SOURCE: Department of Molecular Biology, Cetus Corporation, 1400 53rd Street, Emeryville, CA 94608, USA.
JOURNAL: Gene (65, 1, 13-22) 1988
CODEN: GENED6
LANGUAGE: English
ABSTRACT: A human granulocyte colony stimulating factor (CSF) gene was cloned in Escherichia coli MM294 using plasmid pHCW701 (containing a trpP promoter, to generate plasmid pPD2), or plasmid pFC54.t (containing a pL promoter, to generate **plasmid** pJD1) as expression **vector** . Expression in E. coli was improved by alteration of the 5' sequence of the gene by site-directed mutagenesis.

Initially, no mRNA or protein was detected in the trpP system, and only mRNA was detected in the pL system. When the G+C content was decreased at the 5' end, without altering the predicted protein sequence, mRNA and protein were detected in both systems. Expression reached 17% and 6.5% of total soluble cellular protein in the pL and trpP expression systems, respectively. The N-terminal sequence of the recombinant granulocyte CSF from the pL system was Met-Thr-Pro-Leu-Gly-Pro. Granulocyte CSF isolated from a human LD-1 cell culture did not have an N-terminal methionine residue. Deletion of the threonine codon at the start of the gene for the mature protein resulted in efficient removal of the methionine residue during expression in E. coli. (34 ref)

24/3,AB/44 (Item 11 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0070484 DBR Accession Number: 88-00832 PATENT
New pure human granulocyte colony stimulating factor and muteins - obtained by recombinant DNA methods and expression in bacteria or yeast
PATENT ASSIGNEE: Immunex 1987
PATENT NUMBER: EP 243153 PATENT DATE: 871028 WPI ACCESSION NO.: 87-300791 (8743)
PRIORITY APPLIC. NO.: US 931458 APPLIC. DATE: 861114
NATIONAL APPLIC. NO.: EP 87303509 APPLIC. DATE: 870422
LANGUAGE: English
ABSTRACT: A human granulocyte colony stimulating factor (hG-CSF) in which at least 1 yeast KEX2 protease processing site has been inactivated is new. Specially claimed is an hG-CSF mutein in which Phe-83 of the native sequence has been replaced by Cys, and hG-CSF muteins in which Cys-17 of the native sequence has been replaced by a non-Cys residue. The hG-CSF or its mutein is obtained by culturing a host microorganism carrying an expression vector encoding it. A claimed **vector** is **plasmid** pBC102.K22 (ATCC 67255). The crude product containing hG-CSF is applied to an HPLC column and elution gives the purified product. The mutein may be obtained by coupling amino acids by forming peptide bonds, at least 1 amino acid residue at a yeast KEX2 processing site in the native sequence being inactivated. A DNA sequence coding for the mutein is obtained by oligonucleotide coupling. The products can be obtained in high yields from both bacterial and yeast systems. (38pp)

24/3,AB/45 (Item 12 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0061462 DBR Accession Number: 87-05810
Characterization of **recombinant human granulocyte-colony stimulating** factor produced in mouse cells - cloning in mouse cell culture using **plasmid vector**
AUTHOR: Tsuchiya M; Nomura H; Asano S; Kaziro Y; Nagata S
CORPORATE AFFILIATE: Chugai-Pharm.
CORPORATE SOURCE: Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108, Japan.
JOURNAL: EMBO J. (6, 3, 611-16) 1987

CODEN: EMJODG
LANGUAGE: English
ABSTRACT: Mouse C127I cells were transformed with a chimeric plasmid pTNV2 consisting of bovine papilloma virus DNA and human granulocyte-colony stimulating factor (G-CSF) cDNA placed under the control of the SV40 early promoter. The transformed cells secreted constitutively a high level of human G-CSF, 10-20 ug/ml in a low-serum medium. The secreted G-CSF has been purified to homogeneity by a 2-step procedure including gel filtration and hydrophobic column chromatography. The purified recombinant G-CSF runs as a single band with an apparent mol.weight of 19,000 on SDS PAGE. The **recombinant human G-CSF** was as active as native G-CSF in vitro in supporting proliferation of mouse NFS-60 cells and stimulating colony formation from human as well as mouse bone marrow cells. When the **recombinant human G-CSF** was subcutaneously administrated into mice, a remarkable stimulation of granulopoiesis and splenomegaly was observed. (28 ref)

24/3,AB/46 (Item 13 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0049475 DBR Accession Number: 86-07323
Recombinant human granulocyte colony stimulating factor: effects on normal and leukemic myeloid cells - gene cloning and expression in Escherichia coli
AUTHOR: Souza L M; Boone T C; Gabrilove J; Lai P H; Zsebo K M; Murdock D C
CORPORATE AFFILIATE: AMGen
CORPORATE SOURCE: Amgen, Thousand Oaks, CA 91320, USA.
JOURNAL: Science (232, 4746, 61-65) 1986
CODEN: SCIEAS
LANGUAGE: English
ABSTRACT: The cloning of the gene for human granulocyte colony stimulating factor (hG-CSF) is described. The hG-CSF was purified from the bladder carcinoma cell line 5637 (1A6) and subjected to NH2-terminal amino acid sequence analysis. The region containing amino acids 23-30 was used to produce oligodeoxynucleotide probes of 23 bp, which were complementary to the hG-CSF mRNA with the exception of inosine residues. Probes were labeled and hybridized to filters containing 150,000 cDNA clones constructed from 1A6 poly(A)+ mRNA. The entire insert of plasmid phG-CSF2 from a positive clone was sequenced and the amino acid sequence deduced. An expression vector was constructed to produce sufficient quantities of hG-CSF and Escherichia coli cells containing the p536hG-CSF2 expression plasmid were grown and induced to produce the **recombinant hG-CSF**. When solubilized in a buffer containing sodium laurate and subjected to HPLC, the **recombinant** product was more than 95% pure. The **recombinant** form of **hG-CSF** was tested for its effects on normal and leukemic myeloid cells. (38 ref)

Set	Items	Description
S25	2	PTHKCSF?
S26	2	S25 NOT S23
S27	2	RD (unique items)

Searcher : Shears 571-272-2528

>>>No matching display code(s) found in file(s): 65, 113

27/3,AB/1 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0282424 DBR Accession Number: 2002-02397 PATENT
Recombinant plasmid vector comprising an endo-1,4-beta-D-xylanase signal sequence, human granulocyte-macrophage colony stimulating factor gene and other components, when transformed into microorganism useful for preparing the colony stimulating factor - involving vector plasmid **pTHKCSFmII**-mediated xylanase signal gene transfer for expression in Escherichia coli
AUTHOR: Lee S; Jeong K
CORPORATE SOURCE: Taejon, Korea.
PATENT ASSIGNEE: Korea-Advan.Inst.Sci.Technol. 2001
PATENT NUMBER: WO 200173081 PATENT DATE: 20011004 WPI ACCESSION NO.: 2001-616523 (200171)
PRIORITY APPLIC. NO.: KR 17052 APPLIC. DATE: 20000331
NATIONAL APPLIC. NO.: WO 2001KR549 APPLIC. DATE: 20010331
LANGUAGE: English
ABSTRACT: A recombinant plasmid vector (I) comprising a kanamycin resistance gene (II), a promoter, an endo-1,4-beta-D-xylanase (EC-3.2.1.8) signal sequence, a nucleotide sequence coding for an oligopeptide consisting of 13 amino acids including 6 consecutive histidine residues, and a human granulocyte-macrophage colony stimulating factor gene, is claimed. Also claimed is Escherichia coli transformed with (I) by the vector plasmid **pTHKCSFmII** comprising (II). E. coli transformed with (I) is useful for preparing human granulocyte-macrophage colony stimulating factor. The method comprises culturing the microorganism to obtain a human granulocyte-macrophage colony stimulating factor fusion protein and treating the fusion protein with a protease preferably Factor-X, to obtain a human granulocyte-macrophage colony stimulating factor, where the fusion protein is obtained from the culture by employing Ni-column. (50pp)

27/3,AB/2 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0274926 DBR Accession Number: 2001-15133
High-level secretory production of human granulocyte colony stimulating factor by fed-batch culture of recombinant Escherichia coli - high cell density fermentation, producing secreted recombinant protein
AUTHOR: Yim S C; Jeong K J; Chang H N; +Lee S Y
CORPORATE AFFILIATE: Korea-Advan.Inst.Sci.Technol.
CORPORATE SOURCE: Metabolic and Biomolecular Engineering, National Research Lab., Dept. Chemical Engineering and BioProcess Engineering, KAIST, 373-1 Kusong-dong, Yusong-gu, Taejon 305-701, Korea.
email:leesy@mail.kaist.ac.kr
JOURNAL: Bioprocess and Biosystem Engineering (24, 4, 249-54) 2001
ISSN: 1615-7591 CODEN: 2006C
LANGUAGE: English
ABSTRACT: Escherichia coli MC4100 harbors plasmid **pTHKCSFmII**, which encodes mature human granulocyte colony stimulating factor (hG-CSF)

fused, via a histidine hexamer and Factor-Xa cleavage site, to a Bacillus sp. endo-1,4-beta-xylanase (EC-3.2.1.8) signal peptide. Fed-batch cultures for hG-CSF production were performed in a 2.5 l fermentor, and different feeding strategies (pH-stat, exponential and constant feeding) were compared. Of these, constant feeding of 0.228 g glucose/min and exponential feeding that supported a low specific growth rate (0.116/hr) resulted in the best hG-CSF production (4.4 g/l). For fed-batch cultures performed with the pH-stat and exponential feeding strategies, induction at higher cell density (late exponential phase) resulted in higher hG-CSF production compared with induction at lower cell density. The constant feeding strategy was applied to the scale-up of hG-CSF production to a 30 l fermentor. A maximum dry cell wt of 51.7 g/l and a maximum hG-CSF concentration of 4.2 g/l were obtained. The strategies undertaken will allow development of high cell density fermentations for secretory production of other proteins in E. coli. (21 ref)

Set	Items	Description
S28	58592	AU=(LEE, S? OR LEE S?)
S29	1001	AU=(JEONG, K? OR JEONG K?)
S30	208	S28 AND S29
S31	29	(S28 OR S29 OR S30) AND S3
S32	27	S31 NOT (S25 OR S23)
S33	6	RD (unique items)

-Author (S)

>>>No matching display code(s) found in file(s): 65, 113

33/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

16921639 Document Delivery Available: 000185325800004 References: 17
TITLE: Effect of bacitracin on hGM-CSF production in suspension cultures of transgenic Nicotiana tabacum cells
AUTHOR(S): **Lee SY**; Cho JM; Kim DI (REPRINT)
AUTHOR(S) E-MAIL: kimdi@inha.ac.kr
CORPORATE SOURCE: Inha Univ, Dept Biol Engn, /Inchon 402751//South Korea/ (REPRINT); Inha Univ, Dept Biol Engn, /Inchon 402751//South Korea/
PUBLICATION TYPE: JOURNAL
PUBLICATION: ENZYME AND MICROBIAL TECHNOLOGY, 2003, V33, N4 (SEP 10), P 353-357
GENUINE ARTICLE#: 721PY
PUBLISHER: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA
ISSN: 0141-0229
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Bacitracin, a known protease inhibitor, successfully delayed the rate of proteolytic degradation of recombinant **human granulocytemacrophage colony-stimulating** factor (hGM-CSF). In transgenic Nicotiana tabacum suspension cell cultures, no growth inhibition was observed when at most 500 mg l(-1) bacitracin was added. However, cell growth rate and cell size index were significantly decreased by 1000 mg l(-1) bacitracin and the maximum cell concentration was reduced from 17.1 to 11.2 g l(-1). In terms of hGM-CSF production, all cultures treated with bacitracin showed improved hGM-CSF production, but the protective effect of bacitracin was diminished in relation to culture

time and the decrement of its concentration. Considering both the cell growth and protein production, 500 mg l(-1) bacitracin showed the best results and improved the hGM-CSF production to 112.5 mug l(-1), which was 2.18-fold higher than the 51.5 mug l(-1) of control with no bacitracin. There was no growth retardation or sudden drop in hGM-CSF concentration. The hGM-CSF concentration was increased up to 127.9 mug l(-1) with 1000 mg l(-1) bacitracin, even though this severely inhibited the cell growth.

33/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13382243 References: 21
TITLE: High-level secretory production of human granulocyte-colony stimulating factor by fed-batch culture of **recombinant** Escherichia coli
AUTHOR(S): Yim SC; **Jeong KJ**; Chang HN; **Lee SY (REPRINT)**
AUTHOR(S) E-MAIL: leesy@mail.kaist.ac.kr
CORPORATE SOURCE: Korea Adv Inst Sci & Technol, Yusong Gu, 373-1 Kusongdong/Taejon 305701//South Korea/ (REPRINT); Korea Adv Inst Sci & Technol, Yusong Gu, /Taejon 305701//South Korea/; Korea Adv Inst Sci & Technol, Yusong Gu, /Taejon 305701//South Korea/
PUBLICATION TYPE: JOURNAL
PUBLICATION: BIOPROCESS AND BIOSYSTEMS ENGINEERING, 2001, V24, N4 (NOV), P 249-254
GENUINE ARTICLE#: 509EN
PUBLISHER: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA
ISSN: 1615-7591
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Secretory production of human granulocyte colony-stimulating factor fusion protein (hG-CSF) by fed-batch culture of Escherichia coli was investigated in both 2.5-L and 30-L fermentors, To develop a fed-batch culture condition that allows efficient production of hG-CSF, different feeding strategies including pH-stat, exponential and constant feeding were examined. Among these, the constant feeding strategy (0.228 g glucosexmin(-1)) and the exponential feeding that supports a low specific growth rate (mu=0.116 h(-1)) resulted in the best hG-CSF production. Under these conditions, 4.4 gxL(-1) of hG-CSF was produced. The effect of induction time on the protein production was also investigated. For the fed-batch cultures carried out with the pH-stat and exponential feeding strategies, induction at higher cell density (late-exponential phase) resulted in more hG-CSF production compared with induction at lower cell density (early to mid-exponential phase). The constant feeding strategy that supported best hG-CSF production was applied to the scale-up production of hG-CSF in 30 L of fermentor. The maximum dry cell weight and hG-CSF concentration of 51.7 and 4.2 gxL(-1), respectively, was obtained.

33/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13209671 References: 26

TITLE: Secretory production of human granulocyte colony-stimulating factor in Escherichia coli
AUTHOR(S): **Jeong KJ; Lee SY (REPRINT)**
AUTHOR(S) E-MAIL: leesy@mail.kaist.ac.kr
CORPORATE SOURCE: Korea Adv Inst Sci & Technol, Yusung Gu, 373-1 Kusong Dong/Taejon 305701//South Korea/ (REPRINT); Korea Adv Inst Sci & Technol, Yusung Gu, /Taejon 305701//South Korea/; Korea Adv Inst Sci & Technol, Yusong Gu, /Taejon 305701//South Korea/
PUBLICATION TYPE: JOURNAL
PUBLICATION: PROTEIN EXPRESSION AND PURIFICATION, 2001, V23, N2 (NOV), P 311-318
GENUINE ARTICLE#: 488RN
PUBLISHER: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA
ISSN: 1046-5928
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Human granulocyte colony-stimulating factor (hG-CSF) is a glycoprotein, consisting of 174 amino acids, which plays an important role in hematopoietic cell proliferation, differentiation of hemopoietic precursor cells, and activation of mature neutrophilic granulocytes. In this study, secretory production of hG-CSF in the periplasmic. space of Escherichia coli using the Bacillus sp. endoxylanase signal peptide was examined. For the efficient expression of hG-CSF gene, the first five codons at the N-terminal were altered based on the E. coli high-frequency codon database. The hG-CSF gene fused to the endoxylanase signal sequence was expressed using an inducible trc promoter. However, **recombinant** E. coli cells were completely lysed after induction with I mM isopropyl-beta -D-thiogalacto-pyranoside. Insertion of a small oligopeptide (13 amino acids) containing the histidine hexamer and factor Xa cleavage site between the signal peptide and the mature **hG-CSF** protein allowed successful secretion of **hG-CSF** into the periplasm without cell lysis. Among the several E. coli strains examined, E. coli BL21 (DE3) and E. coli MC4100 allowed production of **hG-CSF** to the highest levels (20-22% of total proteins) with the secretion efficiencies greater than 98%. The circular dichroism spectra showed that the conformation of purified **hG-CSF** is almost identical to native **hG-CSF**. (C) 2001 Academic Press.

33/3,AB/4 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09375723 References: 24
TITLE: Recombinant **human granulocyte colony-stimulating** factor (filgrastim) following high-dose chemotherapy and peripheral blood progenitor cell rescue in high-grade non-Hodgkin's lymphoma: clinical benefits at no extra cost
AUTHOR(S): **Lee SM (REPRINT)**; Radford JA; Dobson L; Huq T; Ryder WDJ; Pettengell R; Morgenstern GR; Scarffe JH; Crowther D
CORPORATE SOURCE: CHRISTIE HOSP NHS TRUST,CRC DEPT MED ONCOL/MANCHESTER M20 4BX/LANCS/ENGLAND/ (REPRINT); CHRISTIE HOSP NHS TRUST,DEPT MED STAT/MANCHESTER M20 4BX/LANCS/ENGLAND/; CHRISTIE HOSP NHS TRUST,DEPT HAEMATOL/MANCHESTER M20 4BX/LANCS/ENGLAND/
PUBLICATION TYPE: JOURNAL

PUBLICATION: BRITISH JOURNAL OF CANCER, 1998, V77, N8 (APR), P1294-1299
GENUINE ARTICLE#: ZG383
PUBLISHER: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND
ISSN: 0007-0920
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: In order to evaluate the potential clinical and economic benefits of granulocyte colony-stimulating factor (G-CSF, filgrastim) following peripheral blood progenitor cells (PBPC) rescue after high-dose chemotherapy (HDCT), 23 consecutive patients aged less than 60 years with poor-prognosis, high-grade non-Hodgkin's lymphoma (NHL) were entered into a prospective randomized trial between May 1993 and September 1995. Patients were randomized to receive either PBPC alone (n = 12) or PBPC+G-CSF (n = II) after HDCT with busulphan and cyclophosphamide. G-CSF (300 mu g day(-1)) was given from day +5 until recovery of granulocyte count to greater than 1.0 x 10(9) l(-1) for 2 consecutive days. The mean time to achieve a granulocyte count > 0.5 x 10(9) l(-1) was significantly shorter in the G-CSF arm (9.7 vs 13.2 days; P<0.0001) as was the median duration of hospital stay (12 vs 15 days; P = 0.001). In addition the recovery periods (range 9-12 vs 11-17 days to achieve a count of 1.0 x 10(9) l(-1)) and hospital stays (range 11-14 vs 13-22 days) were significantly less variable in patients receiving G-CSF in whom the values clustered around the median. There were no statistically significant differences between the study arms in terms of days of fever, documented episodes of bacteraemia, antimicrobial drug usage and platelet/red cell transfusion requirements. Taking into account the costs of total occupied-bed days, drugs, growth factor usage and haematological support, the mean expenditure per inpatient stay was pound 6500 (range pound 5465-pound 8101) in the G-CSF group compared with pound 8316 (range pound 5953-pound 15 801) in the group not receiving G-CSF, with an observed mean saving of pound 1816 per patient (or 22% of the total cost) in the G-CSF group. This study suggests that after HDCT and PBPC rescue, the use of G-CSF leads to more rapid haematological recovery periods and is associated with a more predictable and shorter hospital stay. Furthermore, and despite the additional costs for G-CSF, these clinical benefits are not translated into increased health care expenditure.

33/3,AB/5 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06619813 References: 9
TITLE: HIGH LEVEL EXPRESSION AND SIMPLE PURIFICATION OF RECOMBINANT **HUMAN GRANULOCYTE COLONY-STIMULATING** FACTOR IN E-COLI
AUTHOR(S): KANG SH; NA KH; PARK JH; PARK CI; **LEE SY**; LEE YI
CORPORATE SOURCE: DONG A PHARM CO LTD,RES LABS/KYONGGI DO 449900//SOUTH KOREA/ (Reprint); KOREA UNIV,DEPT AGR CHEM/SEOUL 136075//SOUTH KOREA/; KOREA RES INST BIOSCI & BIOTECHNOL/TAEJON 305606//SOUTH KOREA/
PUBLICATION: BIOTECHNOLOGY LETTERS, 1995, V17, N7 (JUL), P687-692
GENUINE ARTICLE#: RM196
ISSN: 0141-5492
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: A human granulocyte colony-stimulating factor (hG-CSF) gene was synthesized and inserted into a trp expression vector for overexpression in E. coli. A strong expression vector was constructed, and a simple purification procedure including in vitro refolding was estabilished. The final productivity of hG-CSF was 500 similar to 600mg per 1 culture, and the purified hG-CSF showed the proliferation of neutrophils in vivo assays.

33/3,AB/6 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0321376 DBR Accession Number: 2003-22516 PATENT
Producing human granulocyte-colony-stimulating factor (hG-CSF) protein for facilitating secretion and cellular expression comprises using yeast transformed with a vector for protein expression in yeast - involving vector plasmid pLES5-mediated gene transfer and expression in yeast cell
AUTHOR: **LEE S**; LEE K; KIM H; MOON D; JUNG C; LEE Y; **LEE S**
PATENT ASSIGNEE: LG LIFE SCI LTD 2003
PATENT NUMBER: WO 200360141 PATENT DATE: 20030724 WPI ACCESSION NO.: 2003-598538 (200356)
PRIORITY APPLIC. NO.: KR 3289 APPLIC. DATE: 20020121
NATIONAL APPLIC. NO.: WO 2003KR61 APPLIC. DATE: 20030113
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Producing **human granulocyte-colony-stimulating** factor (**hG-CSF**) protein comprising using yeast transformed with a vector for protein expression in yeast, where the vector comprises a nucleotide sequence encoding **hG-CSF** protein. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a synthetic G-CSF gene that comprises a nucleotide sequence of 528 base pairs fully defined in the specification; (2) a vector for protein expression in yeast (pLES 5), where the vector for protein expression in yeast comprises an inducible yeast promoter, a complex secretory signal, a yeast transcription terminator, selection markers, and a yeast replication origin, therefore enhancing the secretion and extracellular expression of secretory **recombinant** protein; (3) a transformed yeast cell (KCTC 10110base pairs), where the vector for **hG-CSF** expression pLES5 ADH2/GAPDH-**hG-CSF** is a vector pLES5 ADH2/GAPDH-G01 comprising inu-alpha-proL-KR(EA)3-GCSF; and (4) producing **hG-CSF** protein by producing **hG-CSF** protein using the yeast cells, and then subjecting the resulting protein to aminopeptidase; or producing **hG-CSF** protein using the yeast cell. BIOTECHNOLOGY - Preferred Method: In producing **hG-CSF** protein, the vector for protein expression in yeast comprises a complex secretory signal sequence, which increases secretion and extracellular expression. The nucleotide sequences of the vector for protein expression in yeast is substituted with yeast preference codons without changing the amino acid sequence, therefore allowing the protein expression to be optimized. The **hG-CSF** is expressed by a synthetic G-CSF gene having a nucleotide sequence of 528 base pairs, fully defined in the specification, in which yeast preference codons are employed. The vector for protein expression in yeast comprises an inducible yeast promoter, a complex secretory

signal, a yeast transcription terminator, selection markers, and a yeast replication origin, therefore enhancing the secretion and extracellular expression of secretory **recombinant** protein. The complex secretory signal comprises a nucleotide sequence encoding the amino acid sequence of 89 amino acids fully defined in the specification. The vector comprises a nucleotide sequence encoding a linking peptide sequence positioned between the complex secretory signal and **hG-CSF** protein. The peptide is selected from Lys-Arg, Lys-Lys, Arg-Lys and Arg-Arg. The vector comprises a nucleotide sequence encoding a peptide positioned between the N-terminal of **hG-CSF** protein sequence and the C-terminal of the complex secretory signal. The peptide consists of a dipeptide Glu and Ala that is repeated not more than six times. The vector comprises a nucleotide sequence encoding naturally-occurring yeast alpha-factor positioned between the N-terminal of **hG-CSF** protein sequence and the C-terminal of the complex secretory signal. USE - The method is useful for producing **hG-CSF** protein for facilitating secretion and extracellular expression. (57 pages)

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